

Form PTO-1390  
(REV. 11-2000)

U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE

ATTORNEY'S DOCKET NUMBER  
9013.43

**TRANSMITTAL LETTER TO THE UNITED STATES  
DESIGNATED/ELECTED OFFICE (DO/EO/US)  
CONCERNING A FILING UNDER 35 U.S.C. 371**

U.S. APPLICATION NO. (If known, see 37 CFR 1.5)

**10/069082**

INTERNATIONAL APPLICATION NO.  
PCT/GB00/03159

INTERNATIONAL FILING DATE  
16 August 2000

PRIORITY DATE CLAIMED  
18 August 1999

TITLE OF INVENTION

Retrovirus Assay

APPLICANT(S) FOR DO/EO/US

Daniel GALBRAITH; Helena KELLY; Kenneth SMITH


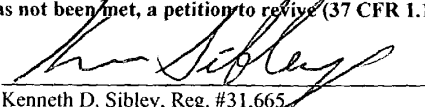
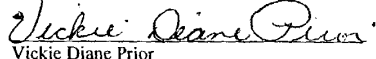
Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:

1. ☒ This is a **FIRST** submission of items concerning a filing under 35 U.S.C. 371.
2. ☐ This is a **SECOND** or **SUBSEQUENT** submission of items concerning a filing under 35 U.S.C. 371.
3. ☐ This is an express request to begin national examination procedures (35 U.S.C. 371(f)). The submission must include items (5), (6), (9) and (21) indicated below.
4. ☐ The US has been elected by the expiration of 19 months from the priority date (Article 31).
5. ☒ A copy of the International Application as filed (35 U.S.C. 371(c)(2))
  - a. ☒ is attached hereto (required only if not communicated by the International Bureau).
  - b. ☐ has been communicated by the International Bureau.
  - c. ☐ is not required, as the application was filed in the United States Receiving Office (RO/US).
6. ☐ An English language translation of the International Application as filed (35 U.S.C. 371(c)(2)).
  - a. ☐ is attached hereto.
  - b. ☐ has been previously submitted under 35 U.S.C. 154(d)(4)
7. ☐ Amendments to the claims of the International Application Under PCT Article 19 (35 U.S.C. 371(c)(3))
  - a. ☐ are attached hereto (required only if not communicated by the International Bureau).
  - b. ☐ have been communicated by the International Bureau.
  - c. ☐ have not been made; however, the time limit for making such amendments has NOT expired.
  - d. ☐ have not been made and will not be made.
8. ☐ An English language translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)).
9. ☐ An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)).
10. ☐ An English language translation of the annexes of the International Preliminary Examination Report Under PCT Article 36 (35 U.S.C. 371(c)(5)).

**Items 11 to 20 below concern document(s) or information included:**

11. ☐ An Information Disclosure Statement under 37 CFR 1.97 and 1.98.
12. ☐ An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.
13. ☒ A **FIRST** preliminary amendment.
14. ☐ A **SECOND** or **SUBSEQUENT** preliminary amendment.
15. ☐ A substitute specification.
16. ☐ A change of power of attorney and/or address letter.
17. ☐ A computer-readable form of the sequence listing in accordance with PCT Rule 13ter.2 and 35 U.S.C. 1.821 - 1.825.
18. ☐ A second copy of the published international application under 35 U.S.C. 154(d)(4).
19. ☐ A second copy of the English language translation of the international application under 35 U.S.C. 154(d)(4)
20. ☐ Other items or information: Written Opinion; International Search Report

1013 Rec'd PCT/PTO 15 JAN 2002

U.S. APPLICATION NO. <b>10/069082</b>		INTERNATIONAL APPLICATION NO. PCT/GB00/03159		ATTORNEY DOCKET NO. 9013.43	
21. <input type="checkbox"/> The following fees are submitted: BASIC NATIONAL FEE (37 CFR 1.492(a) (1) - (5)):  Neither international preliminary examination fee (37 CFR 1.482) nor international search fee (37 CFR 1.445(a)(2)) paid to USPTO and International Search Report not prepared by the EPO or JPO..... <b>\$1040.00</b>  International preliminary examination fee (37 CFR 1.482) not paid to USPTO but International Search Report prepared by the EPO or JPO..... <b>\$890.00</b>  International preliminary examination fee 37 CFR 1.482) not paid to USPTO but international search fee (37 CFR 1.445(a)(2)) paid to USPTO..... <b>\$740.00</b>  International preliminary examination fee (37 CFR 1.482) paid to USPTO but all claims did not satisfy provisions of PCT Article 33(1)-(4)..... <b>\$710.00</b>  International preliminary examination fee (37 CFR 1.482) paid to USPTO and all claims satisfied provisions of PCT Article 33(1)-(4)..... <b>\$100.00</b>				CALCULATIONS      PTO USE ONLY	
ENTER APPROPRIATE BASE FEE AMOUNT =				\$1040.00	
Surcharge of <b>\$130.00</b> for furnishing the oath or declaration later than <input type="checkbox"/> 20 <input type="checkbox"/> 30 months from the earliest claimed priority date (37 CFR 1.492(c)).				\$	
CLAIMS	NUMBER FILED	NUMBER EXTRA	RATE	\$	
Total claims	19 - 20 =	0	x <b>\$18.00</b>	\$	
Independent Claims	1 - 3 =	0	x <b>\$84.00</b>	\$	
MULTIPLE DEPENDENT CLAIM(S) (if applicable)				+ <b>\$280.00</b>	
TOTAL OF ABOVE CALCULATIONS =				\$1320.00	
<input type="checkbox"/> Applicant claims small entity status. See 37 CFR 1.27. The fees indicated above are reduced by 1/2				\$	
SUBTOTAL =				\$1320.00	
Processing fee of <b>\$130.00</b> for furnishing the English translation later than <input type="checkbox"/> 20 <input type="checkbox"/> 30 months from the earliest claimed priority date (37 CFR 1.492(f)).				\$	
TOTAL NATIONAL FEE =				\$1320.00	
Fee for Recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31). <b>\$40.00</b> per property +				\$	
TOTAL FEES ENCLOSED =				\$1320.00	
				Amount to be refunded: \$	
				charged: \$	
a. <input checked="" type="checkbox"/> A check in the amount of <b>\$1320.00</b> to cover the above fees is enclosed.  b. <input type="checkbox"/> Please charge my Deposit Account No. 50-0220 in the amount of \$_____ to cover the above fees. A duplicate copy of this sheet is enclosed.  c. <input type="checkbox"/> The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 50-0220. A duplicate copy of this sheet is enclosed.  d. <input type="checkbox"/> Fees are to be charged to a credit card. <b>WARNING:</b> Information on this form may become public. <b>Credit card</b> <b>information should not be included on this form.</b> Provide credit card information and authorization on PTO-2038.					
<b>NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b)) must be filed and granted to restore the application to pending status.</b>					
SEND ALL CORRESPONDENCE TO:					
 <b>20792</b> PATENT TRADEMARK OFFICE			 Kenneth D. Sibley, Reg. #31,665  Date: <u>February 15, 2002</u>		
<b>CERTIFICATE OF EXPRESS MAILING</b> Express Mail Label No. EV015808902US Date of Deposit: February 15, 2002 I hereby certify that this correspondence is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR 1.10 on the date indicated above and is addressed to: BOX PCT, Attn: DO/EO/US, Commissioner for Patents, Washington, DC 20231.   Vickie Diane Prior					



Rec'd PCT/PTO 30 OCT 2002

Attorney Docket No. 9013.43

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re: Galbraith, et al.  
U.S. Serial No.: 10/069,082  
Int'l Application No.: PCT/GB00/03159  
Int'l Filing Date: August 26, 2000  
For: RETROVIRUS ASSAY

October 25, 2002

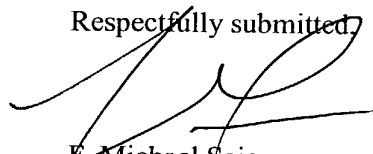
Commissioner for Patents  
Washington, DC 20231

STATEMENT IN SUPPORT OF FILING A  
SEQUENCE LISTING UNDER 37 CFR § 1.821(f)

Sir:

Submitted herewith is a copy of the Sequence Listing in computer readable form. I hereby state that the content of the paper and computer readable copies of the Sequence listing are the same. I also hereby state as required by 37 CFR § 1.821(h) that the computer readable copy submitted concurrently herewith contains no new matter, nor does it go beyond the disclosure of the application as filed.

Respectfully submitted,



E. Michael Sajovec  
Registration No. 31,793

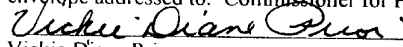


20792

PATENT TRADEMARK OFFICE

**Certificate of Mailing under 37 CFR 1.8**

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner for Patents, Washington, DC 20231, on October 25, 2002.

  
Vickie Diane Prior

Date of Signature: October 25, 2002

IN THE UNITED STATES DESIGNATED OFFICE (DO/US)

In re: Galbraith, et al.  
Serial No. To Be Assigned  
Filed: Concurrently Herewith  
For: RETROVIRUS ASSAY

February 15, 2002

Box PCT  
Attn: DO/US  
Commissioner for Patents  
Washington, DC 20231

**PRELIMINARY AMENDMENT**

Sir:

Prior to the examination of the above application, please amend the above-identified application as follows. If any extension of time for the accompanying response or submission is required, Applicant requests that this be considered a petition therefor. The Commissioner is hereby authorized to charge any additional fee, which may be required, or credit any refund, to our Deposit Account No. 50-0220.

**In the Specification:**

-- RELATED APPLICATIONS

The present application claims priority from International Application No. PCT/GB00/03159, filed on 16 August 2000, which in turn claims priority from British application 9919604.0, filed on 18 August 1999, the disclosures of which are hereby incorporated herein by reference in their entirety.--

**In the Claims:**

Please enter the following amended claims:

13 (amended). An antiserum specific to a polypeptide fragment in accordance with Claim 1.

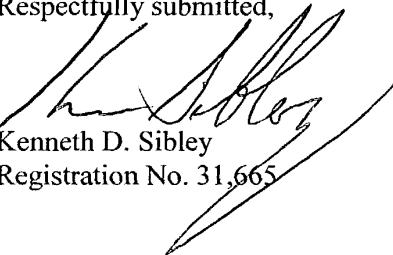
19 (amended). Use of an antibody according to Claim 14, or a polypeptide fragment according to Claim 1 in therapy or diagnosis.

In re: Galbraith, et al.  
International Appl. No. PCT/GB00/03159  
International Filing Date: 16 August 2000  
Page 3

**REMARKS**

Claims 1-19 are presented for examination. The above claims have been amended to better conform to U.S. practice. Applicants respectfully request substantive examination on the merits. A copy of the claims showing the changes made is attached hereto as a "Version with Markings to Show Changes Made".

Respectfully submitted,

  
Kenneth D. Sibley  
Registration No. 31,665



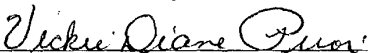
20792

PATENT TRADEMARK OFFICE

**CERTIFICATE OF EXPRESS MAILING**

"Express Mail" mailing label number EL015808902US  
Date of Deposit: February 15, 2002

I hereby certify that this paper or fee is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR 1.10 on the date indicated above and is addressed to Box PCT, Commissioner for Patents, Washington, DC 20231.

  
Vickie Diane Prior

Date of Signature: February 15, 2002

**VERSION WITH MARKINGS TO SHOW CHANGES MADE**

13 (amended). An antiserum specific to a polypeptide fragment in accordance with **[any preceding claim]** Claim 1.

14 (amended). A PoERV specific antibody or fragment thereof raised against a polypeptide fragment in accordance with **[any of]** Claim[s] 1 **[to 12]**.

16 (amended). Use of a polypeptide fragment according to **[any one of]** Claim[s] 1 **[to 12]** in detection of PoERV antibodies in a sample.

18 (amended). An assay kit for use in detection of PoERV antibodies in a sample, the kit comprising a polypeptide fragment in accordance with **[any of]** Claim[s] 1 **[to 12]**.

19 (amended). Use of an antibody according to Claim 14, or a polypeptide fragment according to **[any one of]** Claim[s] 1 **[to 12]** in therapy or diagnosis.

**WO 01/12816**

**PCT/GB00/03159**

**1**

## RETROVIRUS ASSAY

The present invention relates *inter alia* to porcine endogenous retrovirus (PoERV) fragments, in particular to *gag* and *env* fragments of PoERV. The invention relates further to use of such fragments in detection of PoERV or detection of exposure to PoERV. There is also provided antibodies to *gag* and *env* polynucleotides and polypeptides; kits for the detection of PoERV or exposure to PoERV; and *env* peptides and antisera specific for the various types of PoERV and use of such peptides and antisera in the detection of specific PoERV types.

Porcine endogenous retrovirus (PoERV) is an endogenous Gammaretrovirus present typically as a provirus found in several loci in the porcine genome. The proviral genome can be silent or is expressed. Expression of the virus was found to be associated with leukaemic pigs (Strandstrom et al, 1974) and some continuous porcine cell lines produce PoERV (Todaro et al, 1974). Virus from these cells has been shown to infect non-porcine cell-types including human cells (Galbraith et al, 1997; Patience et al, 1997). Three subgroups of PoERV have been described and are designated PoERV A, B and C dependent on the tropism of the virus and the related envelope gene structure (Onions et al, 1998). Only subtypes A and B have been shown to be capable of consistently infecting human cells in vitro. Subgroup C PoERV from mini-pigs has only been shown to infect one human cell line and this may reflect a low capacity for

infection of human cells. Since PoERV is expressed in pigs there is the potential for virus to be present in material prepared from pigs. Furthermore, as a consequence of xenotransplantation using porcine donor organs, there is the possibility that the endogenous virus will be expressed in vivo and be a potential risk of PoERV infection of the patient and the general population thereafter.

A number of different types of PoERV are known, based on their genetic makeup. Types designated PERV A, PERV B, and PoEV1 are described in International Patent Application WO97/40167, while types designated PERV MSL and Tsukuba are described in International Patent Application WO97/21836.

PoERV viruses comprise three genes: *gag*, *pol*, and *env*, generating GAG, POL and ENV polypeptides. It has been observed that the *gag* region of the genome appears to be substantially conserved among different viruses, as well as between PoERV virus types, while the *env* region contains both conserved and non-conserved regions, which non-conserved regions are observed to vary between viral types.

It is among the objects of the present invention to provide means whereby patients and/or samples may be monitored for viral infection. It is further among the objects of the present invention to provide means whereby the viral type may be determined.

According to one aspect of the present invention there is provided a PoERV polypeptide fragment, wherein said polypeptide fragment has PoERV specific antigenic or immunogenic activity. Antigenic or immunogenic activity is

5           According to a further aspect of the present invention  
there is provided an antiserum specific to a PoERV  
polypeptide fragment as described above.

15

20

25

and 3. Conserved regions are those which comprise identical and/or highly conserved amino acid sequences in different PoERV virus types; wholly conserved amino acids are indicated in Figures 2 and 3 by an asterisk beneath the amino acid, with highly conserved amino acids being indicated by a colon. Alternatively, the ENV peptide may be selected from within the non-conserved regions of the various PoERV sequences of Figures 2 and 3, in which case the ENV peptide will be specific for a particular type of PoERV. Specific examples of non-conserved type-specific ENV peptides are shown as peptides D-H and J in Figure 3. In a third embodiment, the ENV peptide may comprise both a conserved and a non-conserved region of the PoERV ENV protein, from either adjacent or non-adjacent regions of the ENV protein. Such peptides may be considered useful in simultaneous detection of any PoERV virus and a specific viral type.

In a further aspect of the present invention, there is provided a fusion GAG/ENV peptide, which peptide comprises both GAG peptide sequences and ENV peptide sequences. Such peptide may be considered useful in simultaneous detection of any PoERV virus, by means of the GAG peptide, and a specific viral type, by means of the ENV peptide.

According to a yet further aspect of the present invention there is provided antibodies specific to either GAG or ENV peptides. The antibodies may be polyclonal or monoclonal. Such antibodies can include, but are not limited to, polyclonal antibodies, monoclonal antibodies

(mAbs), humanized or chimeric antibodies, single chain antibodies, Fab fragments, F(ab')<sub>2</sub> fragments, fragments produced by a Fab expression library, anti-idiotypic (anti-Id) antibodies, and epitope-binding fragments of any of the above. The Ig tails of such antibodies can be modified to reduce complement activation and Fc binding, (See, for example, European Patent No. 239400 B1, Aug. 3, 1994).

For the production of antibodies to a peptide, various host animals can be immunized by injection with a peptide, or a portion thereof. Such host animals can include but are not limited to rabbits, mice, and rats, to name but a few. Various adjuvants can be used to increase the immunological response, depending on the host species, including but not limited to Freund's (complete and incomplete), mineral gels such as aluminum hydroxide, surface active substances such as lysolecithin, pluronic polyols, polyanions, peptides, oil emulsions, keyhole limpet hemocyanin, dinitrophenol, and potentially useful human adjuvants such as BCG (bacille Calmette-Guérin) and *Corynebacterium parvum*.

Polyclonal antibodies are heterogeneous populations of antibody molecules derived from the sera of animals immunized with an antigen, such as target gene product, or an antigenic functional derivative thereof. For the production of polyclonal antibodies, host animals such as those described above, can be immunized by injection with a gene product supplemented with adjuvants as also described above.

Monoclonal antibodies, which are homogeneous populations of antibodies to a particular antigen, can be obtained by any technique which provides for the production of antibody molecules by continuous cell lines in culture.

5 These include, but are not limited to the hybridoma technique of Kohler and Milsrein, (1975, Nature 256:495-497; and US Pat. No. 4,376,110), the human B-cell hybridoma technique (Kosbor et al., 1983, Immunology Today 4:72; Cole et al., 1983, Proc. Natl. Acad. Sci. U.S.A. 80:2026-2030),  
10 and the EBV-hybridoma technique (Cole et al., 1985, Monoclonal Anti-bodies And Cancer Therapy, Alan R. Liss, Inc., pp.77-96).

Such antibodies can be of any immunoglobulin class including IgG, IgM, IgE, IgA, IgD and any subclass thereof.  
15 The hybridoma producing the mAb of this invention can be cultivated in vitro or in vivo. Production of high titers of mAbs in vivo makes this the presently preferred method of production.

In addition, techniques for the production of "chimeric  
20 antibodies" (Morrison et al., 1984, Proc. Natl. Acad. Sci., 81:6851-6855; Neuberger et al., 1984, Nature, 312:604-608; Takeda et al., 1985, Nature, 314:452-454; U.S. Pat. No. 4,816,567) by splicing the genes from a mouse antibody molecule of appropriate antigen specificity together with  
25 genes from a human antibody molecule of appropriate biological activity can be used. A chimeric antibody is a molecule in which different portions are derived from different animal species, such as those having a variable

region derived from a murine mAb and a human immunoglobulin constant region.

Alternatively, techniques described for the production of single chain antibodies (U.S. Pat. No. 4,946,778: Bird, 1988, Science 242:423-426; Huston et al., 1988, Proc. Natl. Acad. Sci. U.S.A. 85:5879-5883; and Ward et al., 1989, Nature 334:544-546) and for making humanized monoclonal antibodies (U.S. Pat. No. 5,225,539) can be utilized to produce anti-differentially expressed or anti-pathway gene product antibodies.

Antibody fragments which recognize specific epitopes can be generated by known techniques. For example, such fragments include but are not limited to: the  $F(ab')_2$  fragments which can be produced by pepsin digestion of the antibody molecule and the Fab fragments which can be generated by reducing the disulfide bridges of the  $F(ab')_2$  fragments. Alternatively, Fab expression libraries can be constructed (Huse et al., 1989, Science, 246:1275-1281) to allow rapid and easy identification of monoclonal Fab fragments with the desired specificity.

Further aspects of the present invention provide methods of screening serum or tissue from humans or animal recipients of porcine tissue for exposure to PoERV. These methods include: use of antibodies to GAG or ENV peptides in the capture and/or detection of PoERV antigens; use of antibodies to GAG or ENV peptides in the detection of PoERV gene expression in virus infected cells by indirect immunofluorescence staining; the use of antibodies to GAG



In an assay for the diagnosis of viral infection, there are basically three distinct approaches that can be adopted, involving the detection of viral nucleic acid, viral antigen or viral antibody respectively. Viral nucleic acid is generally regarded as the best indicator of the presence of the virus itself and would identify materials likely to be infectious. However, the detection of nucleic acid is not usually as straightforward as the detection of antigens or antibodies since the level of target can be very low. Viral antigen is used as a marker for the presence of virus and as an indicator of infectivity. Depending upon the virus, the amount of antigen present in a sample can be very low and difficult to detect. Antibody detection is relatively straightforward because, in effect, the host immune system is amplifying the response to an infection by producing large amounts of circulating antibody. The nature of the antibody response can often be clinically useful, for example IgM rather than IgG class antibodies are indicative of a recent infection, or the response to a particular viral antigen may be associated with clearance of the virus. Thus the exact approach adopted for the diagnosis of a viral infection depends upon the particular circumstances and the information sought. In the case of PoERV, a diagnostic assay may embody any one or a combination of these three approaches.

In an assay for the diagnosis of PoERV involving detection of viral antigen or antibody, the method may comprise contacting a test sample with a peptide of the present invention or a polyclonal or monoclonal antibody  
5 against the peptide and determining whether there is any antigen-antibody binding contained within the test sample. For this purpose, a test kit may be provided comprising a peptide, as defined herein, or a polyclonal or monoclonal antibody thereto and means for determining whether there is  
10 any binding with antibody or antigen respectively contained in the test sample to produce an immune complex. The test sample may be taken from any appropriate tissue or physiological fluid, such as blood (e.g. serum or plasma), saliva, urine, cerebrospinal fluid, sweat, tears or tissue  
15 exudate. If a physiological fluid is obtained, it may optionally be concentrated for any viral antigen or antibody present.

A variety of assay formats may be employed. The peptide can be used to capture selectively antibody against  
20 PoERV from solution, to label selectively the antibody already captured, or both to capture and label the antibody. In addition, the peptide may be used in a variety of homogeneous assay formats in which the antibody reactive with the peptide is detected in solution with no  
25 separation of phases.

The types of assay in which the peptide is used to capture antibody from solution involve immobilization of the peptide on to a solid surface. This surface should be

capable of being washed in some way. Examples of suitable surfaces include polymers of various types (moulded into microtitre wells; beads; dipsticks of various types; aspiration tips; electrodes; and optical devices), particles (for example latex; stabilized red blood cells; bacterial or fungal cells; spores; gold or other metallic or metal-containing sols; and proteinaceous colloids) with the usual size of the particle being from 0.02 to 5 microns, membranes (for example of nitrocellulose; paper; cellulose acetate; and high porosity/high surface area membranes of an organic or inorganic material).

The attachment of the peptide to the surface can be by passive adsorption from a solution of optimum composition which may include surfactants, solvents, salts and/or chaotropes; or by active chemical bonding. Active bonding may be through a variety of reactive or activatable functional groups which may be exposed on the surface (for example condensing agents; active acid esters, halides and anhydrides; amino, hydroxyl, or carboxyl groups; sulphhydryl groups; carbonyl groups; diazo groups; or unsaturated groups). Optionally, the active bonding may be through a protein (itself attached to the surface passively or through active bonding), such as albumin or casein, to which the viral peptide may be chemically bonded by any of a variety of methods. The use of a protein in this way may confer advantages because of isoelectric point, charge, hydrophilicity or other physico-chemical property. The viral peptide may also be attached to the surface (usually

but not necessarily a membrane) following electrophoretic separation of a reaction mixture, such as immunoprecipitation.

After contacting the surface bearing the peptide with  
5 a test sample (in the presence of a blocking mixture if required), allowing time for reaction, and, where necessary, removing the excess of the sample by any of a variety of means, (such as washing, centrifugation, filtration, magnetism or capillary action) the captured  
10 antibody is detected by any means which will give a detectable signal. For example, this may be achieved by use of a labelled molecule or particle as described above which will react with the captured antibody or any molecule containing an epitope contained in the peptide. In one  
15 embodiment, it is preferred to add an anti-human IgG conjugated to horseradish peroxidase and then to detect the bound enzyme by reaction with a substrate to generate a colour.

The detectable signal may be produced by any means  
20 known in the art such as optical or radioactive or physico-chemical and may be provided directly by labelling the molecule or particle with, for example, a dye, radiolabel, fluorescent, luminescent, chemiluminescent, electroactive species, magnetically resonant species or fluorophore, or  
25 indirectly by labelling the molecule or particle with an enzyme itself capable of giving rise to a measurable change of any sort. Alternatively the detectable signal may be obtained using, for example, agglutination, or through a

The labelled peptide may be used in a competitive binding fashion in which its binding to any specific molecule on any of the surfaces exemplified above is blocked by antigen in the sample. Alternatively, it may be used in a non-competitive fashion in which antigen in the sample is bound specifically or non-specifically to any of the surfaces above and is also bound to a specific bi- or

poly-valent molecule (e.g. an antibody) with the remaining valencies being used to capture the labelled peptide.

Examples of the invention will now be described by way of illustration only, and with reference to the accompanying Figures, in which:

Figure 1 is the consensus amino acid sequence of the PoERV GAG protein; Figure 2 is a comparison of amino acid sequences of five different PoERV ENV proteins (PERV; PERV A, PERV B, PoEV 1; Galbraith et al., 1997: PERV MSL, Tsukuba; Fishman, 1997) and Figure 3 is a comparison of amino acid sequences of the variable region of five different PoERV ENV proteins, showing the six different ENV peptides (peptides D-H and J) referred to in the following examples.

#### METHODS

##### Preparation of PoERV virions.

Human 293 cells (American Type Culture Collection [ATCC] # CRL1573) and Raji cells (ATCC # CCL 86 ) were infected with PoERV by exposure to polybrene (Sigma-Aldrich Co. Ltd.) and continued incubation with cell-free filtered supernatant from PK-15 (ATCC # CCL 33) cells previously shown to be infected with all three subgroups of PoERV. The 293 cells allow replication of type B PoERV (POEV-1). The 293 cells were shown to be infected after passage by measurement of the reverse transcriptase activity of the cell supernatant and by a PoERV GAG-specific Polymerase Chain Reaction (PCR). The resulting virus particles were isolated from the cell line supernatant as follows.

WO 01/12816

PCT/GB00/03159

15

Supernatant from exponentially growing cells was layered onto a 20/40% (w/v) discontinuous sucrose density gradient and centrifuged at 100,000 g for 150 min. The viral material at the sucrose interface was harvested, and viral particles pelleted by further ultracentrifugation at 100,000g for 60 min, followed by resuspension in DMEM (Life Technologies Ltd., UK).

#### Control retroviruses

To provide retroviral controls for cross reactivity with PoERV GAG and ENV, Squirrel monkey retrovirus, Murine leukaemia virus, Maedi-Visna virus and Equine infectious anemia virus virions were prepared from the appropriate infected cell line as described by Shepherd and Smith (1999).

#### Selection and preparation of GAG peptides

Peptides from the GAG protein can provide a capture antigen and a means to generate positive control antisera. The antisera can be directed against conserved polypeptides present in the PoERV virion core likely to induce an immune response in recipients of the virus. These reagents would be useful diagnostic tools for immunosurveillance of recipients of porcine material or tissues for exposure to PoERV. Therefore, peptides encompassing potential antigenic regions of PoERV GAG were selected from the translated amino-acids derived from the sequence of the gag region of PoERV based on three criteria; hydrophilicity,

potential  $\beta$ -turns and K, D, R and E charged residues. The regions were identified using Hopp and Woods hydropathicity (1981) scale and Kyte and Doolittle (1982) hydrophobicity scale.

5        For GAG two peptides were identified as potential antigens. Peptide 1 was from the C-terminus of p30-GAG at residue 437-451 of the polypeptide, nucleotides 1896-1940 of the *gag* open reading frame (ORF). Peptide 2 was from the start of the p10 segment of the GAG polypeptide at residue  
10        502-515 of the polypeptide, nucleotides 2091- 2132 of the *gag* ORF. The peptides shown below were chemically synthesised by Genosys Biotechnologies Inc.

Peptide 1:        (C)REERRDRRQEKNLTK

15        Peptide 2:        (W)ARNCPKKGNGPKS

The bracketed amino-acid is not in sequence - 5' position is from next residue (R).

20        These peptides, and the GAG consensus polypeptide sequence, are shown in Figure 1.

25        A BLAST search (Altschui et al., 1997) of the non-redundant GenBank coding sequences with GAG peptide 1 showed homology with seven sequences all from the *gag* ORF. Of the seven, three were with PoERV sequences with accessions gi 3116446 (100% match), emb CAA7651 (100% match), gi 3116442 (86% match). The remainder were against the closely related Gibbon ape leukaemia virus (gi 3033415, 92% match) and Simian sarcoma virus (sp P03330, 86% match).

The remaining two sequences were from murine viruses, including a virus from *Rattus norvegicus* (emb CAA24514; 92% match), and one against *Mus dunni* endogenous retrovirus (gi 3309124, 93% match). A similar BLAST search with GAG peptide 2 showed 100 - 99% homology with only the PoERV sequences listed above.

#### Selection and Preparation of PoERV ENV peptides

We have previously identified and derived the nucleotide sequence of a unique PoERV type capable of infecting human cells (Galbraith, 1997). Furthermore, it has been shown that the amino acid sequence of the ENV region of various PoERV types contains both conserved and non-conserved regions (Galbraith, 1997; Figure 2). In order to exploit these differences to produce immunological reagents to allow the identification of the type of PoERV giving rise to an immunological reaction in a patient, PoERV-type-specific ENV peptides and antisera were generated.

Six peptides, D-H and J, were identified as potential antigens. The peptides are shown below and their position in the env ORF of the various PoERV types is shown in Figure 3. The peptides were chemically synthesised by the University of Glasgow Veterinary Pathology Department.

Peptide D: TSLRPDITQPPSNSTT  
Peptide E: KGKQENIQKWINGMS  
Peptide F: RKTGKYSKVDKWYELGNS  
Peptide G: NTVLTGQRPPTQ

WO 01/12816

PCT/GB00/03159

18

Peptide H: GHGRWKDWQQRVQKDVRNKQIS

Peptide J: IQEQRPSNPNSDYNTT

5 The amino acid residues of all peptides are identified by  
the standard one letter abbreviations.

**Preparation of recombinant PoERV p30-GAG and ENV  
polypeptides**

10 In addition to the peptide reagents more general PoERV p30-  
GAG and an abbreviated ENV polypeptides were designed and  
produced for use as capture antigens and to produce anti-  
polypeptide sera. The required polypeptide portions of the  
gag and env genes were produced by PCR amplification,  
molecularly cloned into a prokaryotic expression vector and  
expressed as described below using standard techniques  
15 (Maniatis et al, 1982).

**PoERV p30-GAG**

20 A fragment encompassing the p30 region of the gag ORF from  
nucleotide 1173-1949 of the PoERV genome (Galbraith et al,  
1997; Gene Bank Accession # A66553) was amplified by PCR  
from cDNA generated from PK15 mRNA using ligation  
independent cloning oligonucleotide primers (pET-32 Ek/LIC  
cloning and expression vector; Novagen Inc. Catalogue #  
69076-3). The oligonucleotides were:

25

**2006年12月**

p30 forward     5' GAC GAC GAC AAG CTG CGC ACC TAT GGC C 3'  
p30 reverse     5' GAG GAG AAG CCC GGG TCT AGG CCA AGA TCT  
TAG TCA AAT TCT TCT C 3'

5     The nucleotides in bold are viral specific.

          The PCR conditions were 30 cycles of 95°C for 1 min,  
58°C for 1 min and 72°C for 1 min. The resulting 776 base  
pair fragment was molecularly cloned into the appropriate  
10     LIC site of the pET-32 LIC vector following the  
manufacturer's instructions (Novagen Inc. 69076-3  
instruction manual), transfected into competent Novoblu<sup>TM</sup>  
*Escherichia coli* cells and plated on solid LB medium  
containing ampicillin. The transformed colonies were  
15     selected by resistance to ampicillin.

#### PoERV ENV

          A fragment encompassing the region of the env ORF from  
nucleotide 5616- 6304 of the PoERV genome (Galbraith et  
20     al,1997; Gene Bank Accession # A66553) was amplified by PCR  
from cDNA generated from PK15 and PoERV-infected 293 cells  
(PoERV B) mRNA using ligation independent cloning  
oligonucleotide primers (pET-32 Ek/LIC cloning and  
expression vector; Novagen Inc. Catalogue # 69076-3). The  
25     oligonucleotides were:

env forward     5' GAC GAC GAC AAG ATC CAT GCA TCC CAC GTT  
3'

25

**Preparation of antisera to whole virions, peptides and recombinant P30-GAG and ENV antigens.**

For ENV peptides D-H and J, the peptides were conjugated with keyhole limpet hemacyanin carrier protein and one sheep was inoculated three times at twenty eight day intervals. The ENV polypeptide was inoculated three times at fourteen day intervals into a rabbit.

25

followed by staining with coomasie brilliant blue dye.  
(Laemmli, 1970; Gallagher, 1997).

Large scale preparations of purified GAG and ENV  
polypeptides were made according to the manufacturer's  
5 instructions (Novagen Inc. Catalogue # 69076-3).

**Preparation of antisera to whole virions, peptides and  
recombinant P30-GAG and ENV antigens.**

For GAG peptide 1 and peptide 2, the peptides were  
10 conjugated with keyhole limpet hemacyanin carrier protein  
and each of two rabbits was inoculated six times at  
fourteen day intervals. The animals were bled out at day  
seventy seven after the first inoculation. The p30-GAG  
polypeptide was inoculated three times at fourteen day  
15 intervals into a rabbit. The animal was bled out at day  
seventy seven.

For ENV peptides D-H and J, the peptides were  
conjugated with keyhole limpet hemacyanin carrier protein  
and one sheep was inoculated three times at twenty eight  
20 day intervals. The ENV polypeptide was inoculated three  
times at fourteen day intervals into a rabbit.

Virions purified from PK15 cells were inoculated three  
times at fourteen day intervals into each of two guinea  
pigs.

### Indirect immunofluorescence staining

To test the specificity of the p30-GAG antisera the method outlined by Riggs (1989) was used. PoERV-infected Raji cells and uninfected control Raji cells were fixed and tested for indirect immunofluorescence with anti p30-GAG using a fluorescein isothiocyanate (FITC) labelled anti-rabbit detector antibody. The cells were examined by fluorescence microscopy.

### Preparation of Western blot membranes

Recombinant p30-GAG polypeptide and ENV polypeptide were prepared, harvested and purified from an *E.coli* vector. The recombinant proteins were tested to determine an appropriate dilution of protein which yielded a positive result in the immunoassay. In addition, extracts from PoERV-infected 293 cells, PoERV-infected Raji cells or purified PoERV virions were used as antigens. To obtain specific and reproducible Western blot assays, a number of parameters were required to be optimised for each assay, such as: Primary antibody dilution, incubation time, incubation temperature, secondary antibody dilution, incubation time, incubation temperature, washing buffers, blocking/dilution buffers, developing reagents. Recombinant polypeptides were added to nine wells of a ten lane 12% Tris/glycine acrylamide gel. Molecular weight markers were added to the first lane. The samples were electrophoresed and the gel electroblotted to a polyvinylidene fluoride (PVDF) membrane. (Gallagher et al,

1997). The membrane was cut into strips each strip containing one lane of recombinant protein. These strips were used as the basis of the assay.

5 **Preparation dilutions of antisera**

Samples were prepared in a Class 2 safety cabinet or other clean environments.

10 A typical negative control was prepared by making up to a 1:200 dilution of normal sera in blocking reagent.

A typical positive control was prepared by making a 1: 500, 1: 1000 or greater dilution of anti-PoERV p30-GAG polypeptide, peptide serum or anti - recombinant ENV serum.

15

A typical test serum was prepared by making up to a 1:200 dilution of sera.

20 **Preparation of Western blotting membranes and PoERV antibody detection.**

To block non-specific binding sites membrane strips each were placed in a 15 ml centrifuge tube and 2 ml blocking reagent (2.5 g skimmed dried milk in 50 ml PBS/ 0.5% v/v Tween-20<sup>TM</sup>) added. The strips were placed on a rotary  
25 shaker such that the strip moved slightly on each revolution and were incubated for 30 min at ambient

temperature. The blocking reagent was removed and replaced with 5-10  $\mu$ l of the diluted serum. The membrane was incubated with shaking for 1 h at ambient temperature. To stop incubation the strip was removed from diluted serum and placed into PBS/ Tween-20™ and washed with three changes of PBS/ Tween-20™ at ambient temperature with shaking.

The appropriate species specific secondary antiserum conjugated to alkaline phosphatase was used as detector e.g. if human serum was being tested, an anti-human IgG alkaline phosphatase (AP) conjugate was used. The p30-GAG positive control required anti-rabbit IgG AP conjugate for detection and the anti ENV required anti-sheep IgG AP conjugate. The detection was done as follows; each strip was placed in an unused 15 ml centrifuge tube, 2 ml of 1:1000 dilution of secondary sera in blocking reagent was added and incubated with shaking at ambient temperature for 1 h. The strip was removed from the centrifuge tube, placed in PBS/Tween-20™ and washed with 3 changes of PBS/Tween-20™, at ambient temperature with shaking. The strips were then put into a 15 ml centrifuge tube and 2 ml of bromochlorindoyl phosphate/ nitroblue tetrazolium (BCIP/NBT, Sigma-Aldrich Co. Ltd.) solution was added to each tube. The strips were shaken gently and allowed to develop for 5 min. The reaction was stopped by rinsing the membrane strip in purified water and the strips were removed from the water and allowed to air dry.

# **ENZYME-LINKED IMMUNOSORBENT ASSAY (ELISA)**

## **Antigen coating of microtiter plates**

50  $\mu$ l of antigen (either recombinant p30-GAG, extracts from PoERV-infected 293 cells or purified PoERV B virions) were diluted to the required concentration in carbonate-bicarbonate coating buffer (Sigma-Aldrich Co. Ltd.) was added to wells of a 96 well, flat bottomed microtiter ELISA plate (Dynex Immulon 2). Some wells contained carbonate-bicarbonate coating buffer only and some were left blank to act as controls for non-specific binding. The plate was covered with a plate seal and incubated at 4°C for approximately 16 h. The unbound antigen and coating solution were then removed from the wells with a pipette and washed three times with PBS / 0.05% Tween-20™. Any remaining PBS / 0.05% Tween-20™ was removed by blotting on a tissue.

## **Blocking of microtiter plates**

50  $\mu$ l of fresh blocking buffer (5% (w/v) skimmed milk /PBS / 0.05% Tween-20™) was added to each antigen coated well and control well. The plate was covered with a plate seal and incubated at ambient temperature in an humidified chamber for 1 h. The blocking buffer was removed and the plate wells washed three times with PBS / 0.05% Tween-20™ and any remaining PBS / 0.05% Tween-20™ was removed by blotting on a tissue.

**Incubation with primary antibody**

50  $\mu$ l of negative control sera, test sera, and positive control sera at the experimental dilution were added to the antigen coated wells and the plates covered with a plate seal and incubated at ambient temperature for approximately 1 h in an humidified chamber. Following incubation all sera were removed using a pipette and the plate wells washed three times with PBS / 0.05% Tween-20™, any remaining PBS / 0.05% Tween-20™ was removed by blotting on a tissue.

**Incubation and development with peroxidase-conjugated secondary antibody**

50  $\mu$ l of a 1:500 dilution of species specific peroxidase conjugated secondary antibody in blocking buffer was added to each antigen coated well. For human serum an anti-human IgG peroxidase conjugate was used. The p30-GAG positive control required anti-rabbit IgG peroxidase conjugate for detection and the anti ENV required anti-sheep IgG peroxidase conjugate. The plates were covered with a plate seal and incubated at ambient temperature for approximately 1 h in an humidified chamber. Following incubation the conjugate was removed using a pipette and the plate wells washed three times with PBS / 0.05% Tween-20™. Any remaining PBS / 0.05% Tween-20™ was removed by blotting on a tissue.

The substrate was prepared as follows: one O-phenylenediamine tablet (Sigma-Aldrich Co. Ltd.) and one urea/H<sub>2</sub>O<sub>2</sub> tablet were dissolved in 20 ml of purified water.

An aliquot of 50  $\mu$ l of substrate was added to each well and the plate incubated at ambient temperature in the dark for 30 min. The reaction was then stopped by adding 50  $\mu$ l of 3N HCl or 3 M H<sub>2</sub>SO<sub>4</sub> to each well. The colour development in the wells was measured at 490 nm using a Dynex MRX microplate reader.

For alkaline phosphatase conjugated secondary antibodies the substrate used was p-Nitrophenyl phosphate (pNPP; Sigma-Aldrich Co. Ltd.) and the plates were read at 405 nm.

#### Electron Microscopy

Negative stain electron microscopy (NSEM) (Doane, 1980) was used to identify the presence of PoERV virions. Supernatant from PoERV-infected pK15 cells was layered onto a 20/40% (w/v) discontinuous sucrose density gradient and centrifuged at 100,000 g for 150 min. The viral material at the sucrose interface was harvested, and viral particles pelleted by further ultracentrifugation at 100,000g for 60 min, followed by resuspension in DMEM (Life Technologies Ltd.). The sample was then applied to pioloform-coated copper 300 mesh EM grids and allowed to air dry. Grids were fixed with 2.5% glutaraldehyde (Agar Scientific), stained with 5% uranyl acetate (Agar Scientific) and allowed to air dry. Grids were examined on a Philips EM-400 transmission electron microscope.

**Immuno- Electron Microscopy**

The immunostaining was done following the method of Marshall et al (1992). Briefly, NSEM samples were applied to pioloform-coated nickel 300 mesh EM grids and allowed to  
5 air dry. Grids were fixed with modified immunofix, post fixed with 0.5 M  $\text{NH}_4\text{Cl}$ , then incubated with 2% bovine serum albumin (Sigma-Aldrich Co. Ltd.). Samples were then incubated with rabbit anti-PoERV (rabbits immunised with whole PoERV) or rabbit anti-PoERV p30-GAG antibody, washed  
10 in modified immunobuffer followed by incubation with anti-rabbit IgG gold conjugate (Sigma-Aldrich Co. Ltd.). Grids were stained with 5% uranyl acetate, and allowed to air dry. Samples were visualised on a Philips EM-400 transmission electron microscope.

15

**EXAMPLE ONE**

**Indirect immunofluorescence staining of PoERV-infected cells.**

20 Viral specific fluorescence was observed in PoERV-infected Raji cells using the anti p30-GAG antiserum. No immunofluorescence was seen with the negative control Raji cells.

25

**EXAMPLE TWO****Western Blotting for Antibodies to PoERV GAG**

Anti-GAG peptide 1 antisera and sera from rabbits  
5 inoculated with the recombinant p30-GAG polypeptide  
detected the expected protein of approximately 30kd in  
extracts of PoERV-infected 293 or PoERV-infected Raji  
cells, purified PoERV virions and recombinant p30-GAG. The  
PoERV antibody could be detected at a dilution of 1:1000.

10

No band of equivalent size to the GAG 30 kd polypeptide was  
detected in uninfected control cells.

15

No band of equivalent size to the GAG 30 kd polypeptide was  
detected against the following purified retroviruses:

Squirrel monkey retrovirus

Murine leukaemia virus

Maedi-Visna virus

20

Equine infectious anemia virus

Therefore, the positive control antisera were specific for  
PoERV.

25

**Determination of assay specificity using Serum Panels****Normal human sera**

On testing of 90 normal serum samples from healthy  
individuals, whose blood was taken for occupational health

reasons, no PoERV reactive antibody was detected in any of the sera.

#### Normal primate sera

On testing 42 normal serum samples from healthy primates no  
5 PoERV reactive antibody was detected. There was no cross-reactivity with sera from normal primates.

#### Cardiac transplant patient sera

On testing 20 serum samples from individuals who had  
10 received a cardiac transplant in the preceding 36 months no PoERV reactive antibody was detected. There was no cross-reactivity with sera from patients who had been immunosuppressed.

#### HIV positive sera

15 On testing 13 serum samples from individuals positive for the presence of antibody to HIV no PoERV reactive antibody was detected. There was no cross-reactivity with sera from patients infected with a human Lentivirus.

#### 20 HTLV positive sera

On testing 10 serum samples from individuals positive for the presence of antibody to HTLV-1 virus no PoERV reactive antibody was detected. There was no cross-reactivity with sera from patients infected with a human Gammaretrovirus.

**Butchers with acute lymphoblastic leukaemia (ALL)**

On testing 3 serum samples from butchers with ALL no PoERV reactive antibody was detected. There was no cross-reactivity with sera from patients with assumed prolonged exposure to PoERV and PoERV antigens with a leukaemic disorder.

**EXAMPLE THREE****ELISA p30-GAG**

A titration of p30-GAG antigen to anti-p30-GAG antisera gave a significant signal at 1:250600 dilution antigen to 1:32000 dilution of antisera. A similar titration of antisera against PoERV virions gave a significant signal at a 1:3200 dilution of both antigen and antisera.

**Normal human sera**

On testing of five normal serum samples from healthy individuals whose blood was taken for occupational health reasons, no significant signal was detected in any of the sera against recombinant p30-GAG.

**EXAMPLE FOUR****Detection and Visualisation of PoERV Virions by Immuno-Electron Microscopy**

Examination of PoERV virion preparations by negative stain revealed particles showing the characteristic size and structure of a Gammaretrovirus of approximately 90-120 nm with a dark inner core and double membraneous outer region.

The particles bound immuno-gold labeled anti p30-GAG antiserum indicating that the antiserum could be used to visualise PoERV virions by immuno-electron microscopy.

## 5      **EXAMPLE FIVE**

### **ELISA ENV**

A titration of antisera raised against ENV peptides D, E, F, G, H, J. to purified PoERV B virions gave a significant signal indicating that the ENV peptides produced a virus-specific reaction in the animals. Peptides D and F, both  
 10      from PoERV B (POEV1; Figure 2; Galbraith et al, 1997) gave the highest signal.

## **EXAMPLE SIX**

### 15      **Western Blotting for Antibodies to PoERV ENV**

Antisera from guinea pigs inoculated with whole purified PoERV virions from PK15 cells detected the expected recombinant ENV protein of approximately 24 kD in extracts of *E.coli* expressing the env construct.

20      No band of equivalent size to the ENV 24 kD polypeptide was detected on *E.coli* control cells without the expression construct.

**REFERENCES**

- Altschui SF, Madden TL, Schaffer AA, Zhang J, Zhang Z,  
Miller W and Lipman DJ (1997). Gapped BLAST and PSI-BLAST:  
5 a new generation of protein database search programs.  
Nucleic Acids Research, 25: 3389-3402.
- Doane FW . (1980). Virus morphology as an aid for rapid  
diagnosis. Yale Journal of Biological Medicine, 53, 19-25.
- 10 Ekins RP. (1997). Immunoassay design and optimisation. In  
Principles and Practice of Immunoassay Second Edition. Ed.  
CP Price and DJ Newman. Macmillan Reference, Ltd. London.
- 15 Fishman JA. (1997). Patent Application WO97/21836.
- Galbraith DN. Haworth C, Lees GM, and Smith KT. (1997).  
Patent Application WO97/40167.
- 20 Gallagher S. (1997). One-dimensional SDS gel  
electrophoresis of proteins. In Current Protocols in  
Molecular Biology. 10.2.2-10.2.35. John Wiley & Sons, Inc.  
USA.
- 25 Gallagher S, Winston SE, Fuller SA and Hurrell JGR. (1997).  
Immunoblotting and immunodetection. In Current Protocols in  
Molecular Biology. 10.8.1-10.8.21. John Wiley & Sons, Inc.  
USA.

- Hopp TP and Woods KR. (1981). Prediction of protein antigenic determinants from amino acid sequences. Proceeding of the National Academy of Sciences USA, 78, 3824-3828.
- 5 Kyte J and Doolittle RF. (1982). A simple method for displaying the hydropathic character of a protein. Journal of Molecular Biology, 157, 105-132.
- 10 Laemmli UK. 1970). Cleavage of structural proteins during the assembly of the head of bacteriophage T4. Nature, 227, 680-685.
- 15 Maniatis T, Fritsch EF and Sambrook J. (1982). Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Laboratory, Cold Spring Harbor, NY.
- 20 Marshall GE, Kontas AG, Reid GG, Edwards JG and Lee WR. (1992). Type IV collagen and laminin in Bruch's membrane and basal linear deposit in the human macula. British Journal of Ophthalmology, 76, 607-614.
- 25 Onions D, Hart D, Mahoney C, Galbraith D and Smith K. (1998). Endogenous retroviruses and the safety of porcine xenotransplantation. Trends in Microbiology, 6, 430-431.
- Patience C, Takeuchi Y and Weiss R. (1997). Infection of human cells by an endogenous virus of pigs. Nature

Medicine, 3, 282-286.

5 Riggs JL. (1989). Immunofluorescence staining. In  
Diagnostic Procedures for Viral, Rickettsial and Chlamydial  
Infections Sixth Edition. Ed. NJ Schmidt and RW Emmons.  
123-133. American Public Health Association Inc. Washington  
DC.

10 Strandstrom H, Veijalainen P, Moennig V, Hunsmann G,  
Schwarz H and Schafer W. (1974). C-type particles produced  
by a permanent cell line from a leukemic pig. 1. Origin and  
properties of the host cells and some evidence for the  
occurrence of C-type particles. Virology, 57, 175-178.

15 Shepherd AJ and Smith KT. (1999). Viral evaluation of  
animal cell lines used in biotechnology. In Methods in  
Biotechnology, Vol. 8: Animal Cell Biotechnology. Ed. N  
Jenkins. Humana Press, Inc. Totwa New Jersey.

20 Todaro GJ, Benveniste RE, Lieber MM, and Sher CJ. (1974).  
Characterisation of a type C virus released from the  
porcine cell line PK (15). Virology, 58, 65-74.

CLAIMS

1. A porcine endogenous retrovirus (PoERV) polypeptide fragment, wherein said polypeptide fragment has PoERV specific antigenic or immunogenic activity.
- 5 2. A polypeptide fragment according to claim 1, wherein said polypeptide fragment comprises a fragment of a PoERV GAG polypeptide.
- 10 3. A polypeptide fragment according to claim 2, wherein said polypeptide fragment comprises a fragment of a polypeptide sequence as shown in Figure 1.
- 15 4. A polypeptide fragment according to claim 3, wherein said polypeptide fragment comprises the amino acid sequence REERRDRRQEKNLTK.
- 20 5. A polypeptide fragment according to claim 3, wherein said polypeptide fragment comprises the amino acid sequence ARNCPKKGNKGPKV.
6. A polypeptide fragment according to claim 1, wherein said polypeptide fragment comprises a fragment of a PoERV ENV polypeptide.
- 25 7. A polypeptide fragment according to claim 6 wherein said polypeptide fragment comprises a fragment of a polypeptide sequence as shown in Figures 2 or 3.

8. A polypeptide fragment according to claim 7 wherein said polypeptide fragment comprises a fragment from within a conserved region of the sequences shown in Figures 2 and 3.

5

9. A polypeptide fragment according to claim 7 wherein said polypeptide fragment comprises a fragment from within a non-conserved region of the sequences shown in Figures 2 and 3.

10

10. A polypeptide fragment according to claim 9 wherein said polypeptide fragment comprises an amino acid sequence selected from the sequences of peptides D, E, F, G, H and J as shown in Figure 3.

15

11. A polypeptide fragment according to claim 7 wherein said polypeptide fragment comprises a fragment from within a conserved region of the sequences shown in Figures 2 and 3, and a fragment from within a non-conserved region of the sequences shown in Figures 2 and 3.

20

12. A polypeptide fragment according to claim 1, wherein said polypeptide fragment comprises a fragment of a PoERV GAG polypeptide and a fragment of a PoERV ENV polypeptide.

25

13. An antiserum specific to a polypeptide fragment in accordance with any preceding claim.

14. A PoERV specific antibody or fragment thereof raised against a polypeptide fragment in accordance with any of claims 1 to 12.

5 15. Use of an antibody according to claim 14 in the detection of PoERV in a sample.

10 16. Use of a polypeptide fragment according to any one of claims 1 to 12 in the detection of PoERV antibodies in a sample.

15 17. An assay kit for use in detection of PoERV in a sample, the kit comprising an antibody in accordance with claim 14.

18. An assay kit for use in detection of PoERV antibodies in a sample, the kit comprising a polypeptide fragment in accordance with any of claims 1 to 12.

20 19. Use of an antibody according to claim 14, or a polypeptide fragment according to any one of claims 1 to 12 in therapy or diagnosis.

25

10069022 103002

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization  
International Bureau



(43) International Publication Date  
22 February 2001 (22.02.2001)

PCT

(10) International Publication Number  
**WO 01/12816 A2**

(51) International Patent Classification<sup>7</sup>: C12N 15/49,  
C07K 14/15, G01N 33/50, C07K 16/10, A61K 39/21

(74) Agents: MCCALLUM, William, Potter et al.; Cruik-  
shank & Fairweather, 19 Royal Exchange Square, Glasgow  
G1 3AE (GB).

(21) International Application Number: PCT/GB00/03159

(22) International Filing Date: 16 August 2000 (16.08.2000)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:  
9919604.0 18 August 1999 (18.08.1999) GB

(71) Applicant (for all designated States except US): QUIP  
TECHNOLOGY LIMITED [GB/GB]; Todd Campus,  
West of Scotland Science Park, Glasgow G20 0XA (GB).

(81) Designated States (national): AE, AG, AL, AM, AT, AU,  
AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ,  
DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,  
HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,  
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ,  
NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM,  
TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.

(84) Designated States (regional): ARIPO patent (GH, GM,  
KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian  
patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European  
patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE,  
IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG,  
CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

(72) Inventors; and

(75) Inventors/Applicants (for US only): GALBRAITH,  
Daniel [GB/GB]; 513 Alexandra Parade, Glasgow G31  
3EW (GB). KELLY, Helena [GB/GB]; Flat 1/2, 19  
Kelvindale Gardens, Glasgow G20 8DW (GB). SMITH,  
Kenneth [GB/GB]; 5 Capelrig Lane, Newton Mearns,  
Glasgow G77 6XZ (GB).

Published:

— Without international search report and to be republished  
upon receipt of that report.

For two-letter codes and other abbreviations, refer to the "Guid-  
ance Notes on Codes and Abbreviations" appearing at the begin-  
ning of each regular issue of the PCT Gazette.

(54) Title: RETROVIRUS ASSAY

**PoERV GAG POLYPEPTIDE SHOWING POSITIONS OF PEPTIDES**

MGQTVTTPLSLTLDHWTEVRSRAHNLSVQVKKGPWQTFCASEWPTFDVGWPSEGTFNSEIILAVKAIIFQ  
TGPESHDPQEPYILTWQDLAEDPPPVWKPWLNKPRKPGPRILALGEKNKHSAEKVEPSSSYLPRDRGAAD  
LAGTPCSPPTLSSTGCCEGTSAPPGAPVVEGPAAGTRSRRGATPERTDEIAILPLRTYGPMPGGQLQP  
LQYWPFSADLYNWKTNHPPFSEDPQRLTGLVESLMFSSHQPTWDDCQQLLTFTTEERERILLEARKNV  
PGADGRPTQLQNEIDMGFPLTRPGWDYNTAEGRESLKIYQALVAGLRGASRRPTNLAKVREVMQGPNEP  
PSVFLERLMEAFRRFTPFDPSTSEAKASVALAFIQSALDIRKKLQRLQELQEAELRDLVREAEKVYYRR  
ETEEKEQKKEKEREERERRRRQEKNTKILAAVVEGKSSRERERDFRKIRSGPRQSGNLGNRTPLDK  
DCCAYCKEKGHWARNCPKKGNGKPKVLALAEEDKD

The gag peptides 1 and 2 are shown in lower case bold. Peptide 1:  
REERRDRRQEKNTK; Peptide 2: ARNCPKKGNGKPKV.

(57) Abstract: The present invention relates to polypeptide fragments derived from porcine endogenous retrovirus (PoERV) GAG and ENV polypeptides, and to their use in detection of PoERV antibodies in a test sample. Also provided are antibodies to GAG and ENV polypeptides, which may be used to detect PoERV in a sample. Polypeptide sequences are provided which are common to several strains of PoERV, as are sequences specific to a single PoERV strain.



WO 01/12816 A2

1/4

MGQTVTTPLSLTLDHWTEVRSRAHNLSVQVKKGPWQTFCASEWPTFDVGWPSEGTFNSEIILAVKAIIFQ  
TGPGSHPDQEPYILTWQDLAEDPPPWWKPWLNKPRKPGPRILALGEKNKHSAEKVEPSSSYLPRDRGAAD  
LAGTPTCSPTPLSSTGCCEGTSAPPVVEGPAAGTRSRRGATPERTDEIAILPLRTYGPPMPGGQLQP  
LQYWPFSSADLYNWKTNHPPFSEDPQRLTGLVESLMFSHQPTWDDCQQLLQTLFTTEERERILLEARKNV  
PGADGRPTQLQNEIDMGFPLTRPGWDYNTAEGRESLKIYRQALVAGLRGASRRPTNLAKVREVMQGPNEP  
PSVFLERLMEAFRRFTPFDPTSEAQKASVALAFIQSALDIRKKLORLEGLQEAELRDLVREAEKVYYRR  
ETEEEKEQRKEKEREEREerrdrqeknltkILAAVVEGKSSRERERDFRKIRSGPRQSGNLGNRTPLDK  
DQCAYCKEKGHWarncpkkgkgnkpkvLLEEDKD

FIGURE 1

10/069082

2/4

PERVA MHPTLSRRHLPIRGGKPKRLKIPLSFASIAWFLTSLITPQVNGKRLVDSPNSHKPLSLTW  
 POEVMSL MHPTLNRRHLPIRGGKPKRLKIPLSFASIAWFLTSLITSQTNGMRIGDSLNSHKPLSLTW  
 TSUKUBA MHPTLSRRHLPIRGGKPKRLKIPLSFASIAWFLTSLITSQTNGMRIGDSLNSHKPLSLTW  
 PERVB MHPTLSWRHLPTRGGEPKRLRIPLSFASIAWFLTLTITPQASSKRLIDSSNPHRPLSLTW  
 POEV1 MHPTLSRRHLPTRGGEPKRLRIPLSFASIAWFLTLTITPQASSKRLIDSSNPHRPLSLTW  
 \*\*\*\*\* : \* : \*\*\*\*\* : \*\*\*\*\* : \* : \* : \* : \*\*\*\*\*

PERVA LLTDSGTGININSTQGEAPLGTWWPELYVCLRSVIPGLNDQATPPDVLRAYGFYVCPGPP  
 POEVMSL LITDSGTGININNTQGEAPLGTWWPDLYVCLRSVIPSL---TSPDPILHAHGFYVCPGPP  
 TSUKUBA LITDSGTGININNTQGEAPLGTWWPDLYVCLRSVIPSL---TSPDPILHAHGFYVCPGPP  
 PERVB LIIDPDTGVTVNSTRGVAPRGTTWWPELHFCLRLINPAVK--STPPNLVRSYGFYCCPG-T  
 POEV1 LIIDPDTGVTVNSTRGVAPRGTTWWPELHFCLRLINPAVK--STPPNLVRSYGFYCCPG-T  
 \* : \* : \* : \* : \* : \* : \* : \* : \* : \* : \* : \* : \* : \* : \* : \*

PERVA NNEEYCGNPQDFFCKQWSCITSNDGNWKWPVSQQDRVSYSFVNNTPTSYNQFNYGHGRWKD  
 POEVMSL NNGKHCGNPRDFFCKQWNCVTSNDGYWKWPTSQQDRVSFSYVNTYTSSGQFNY-----LT  
 TSUKUBA NNGKHCGNPRDFFCKQWNCVTSNDGYWKWPTSQQDRVSFSYVNTYTSSGQFNY-----LT  
 PERVB EKEKYCGSGESFCRRWSCVTSNDGDWKWPI SLQDRVKFSFVNSG--PGKYKVMK-----  
 POEV1 EKEKYCGSGESFCRRWSCVTSNDGDWKWPI SLQDRVKFSFVNSG--PGKYKMMK-----  
 : : \* : \* : \* : \* : \* : \* : \* : \* : \* : \* : \* : \*

PERVA WQORVQKDVRNKQISCHSLDLDYLKISFTE--KGKQENIQKWVNGISWGIVYGGSGRKK  
 POEVMSL W-----IRTGSPKCSPSDLDYLKISFTE--KGKQENILKWVNGMSWGMVYGGSGKQP  
 TSUKUBA W-----IRTGSPKCSPSDLDYLKISFTE--KGKQENILKWVNGMSWGMVYGGSGKQP  
 PERVB -----LYKDKSCSPSDLDYLKISFTE--KGKQENIQKWINGMSWGMVYFYKYGGG-A  
 POEV1 -----LYKDKSCSPSDLDYLKISFTE--KGKQENIQKWINGMSWGMVYFYKYGGG-A  
 . \* . \*\*\*\*\* . \* : : \* . \* : \*

PERVA GSVLTIRLRIETQMEPPVAIGPNKGLAEQGPPPIEQRP-SPNPSD-----YNTT  
 POEVMSL GSILTIRLKIN-QLEPPMAIGNTVLTGQRPPTQ-----GPGPS-----SNIT  
 TSUKUBA GSILTIRLKIN-QLEPPMAIGNTVLTGQRPPTQ-----GPGPS-----SNIT  
 PERVB GSTLTIRLRIETGTEPPVAVGPDVLAEGQPPALEPPHNLPVLPQTLRDPITQPPSNGT  
 POEV1 GSTLTIRLRIETGTEPPVAMGPDVLAEGQPPALEPPHNLPVLPQTLRDPITQPPSNST  
 \*\* \*\*\*\*\* : \* : \* : \* : \* : \* : \* : \* : \* : \*

PERVA SGSVPT-----EPNITIKTGAKLFSLIQGAFOALNSTTPEATSSCWLCCLASGPPYYEGMA  
 POEVMSL SGSDPT-----ESNSTTKMGAKLFSLIQGAFOALNSTTPEATSSCWLCCLASGPPYYEGMA  
 TSUKUBA SGSDPT-----ESSSTTKMGAKLFSLIQGAFOALNSTTPEATSSCWLCCLALGPPYYEGMA  
 PERVB TGLIPTNTPRNSPGVPVKTGQRLFSLIQGAFOALNSTDPDATSSCWLCCLSSGPPYYEGMA  
 POEV1 TGLIPTNTPRNSPGVPVKTGQRLFSLIQGAFOALNSTDPDATSSCWLCCLSSGPPYYEGMA  
 : \* . . . . \* : \*\*\*\*\* : \*\*\*\*\* : \*\*\*\*\* : \*\*\*\*\* : \*

PERVA RGGKFNVTKHRDQCTWGSQNKLTLETVSGKGTICIGMVPPSHQHLCNHTAFNRTSESOY  
 POEVMSL RRGKFNVTKHRDQCTWGSQNKLTLETVSGKGTICIGKVPPSHQHLCNHTAFNQTSESOY  
 TSUKUBA RRGKFNVTKHRDQCTWGSQNKLTLETVSGKGTICIGKVPPSHQHLCNHTAFNQTSESOY  
 PERVB KEGKFNVTKHRNQCTWGSRNKLTLETVSGKGTICIGKAPPSHQHLCYSTVVEQASENQY  
 POEV1 KERKFNVTKHRNQCTWGSRNKLTLETVSGKGTICIGKAPPSHQHLCYSTVVEQASENQY  
 : \*\*\*\*\* : \* : \*\*\*\*\* : \*\*\*\*\* : \*\*\*\*\* : \*\*\*\*\* : \*\*\*\*\* : \*

PERVA LVPGYDRWWACNTGLTPCVSTLVFNQTKDFCVMVQIVPRVYHPEEVLDEYDYNRNP  
 POEVMSL LVPGYDRWWACNTGLTPCVSTLVFNQTKDFCVMVQIVPRVYHPEEVLDEYDYNRNP  
 TSUKUBA LVPGYDRWWACNTGLTPCVSTLVFNQTKDFCVMVQIVPRVYHPEEVLDEYDYNRNP  
 PERVB LVPGYNRWWACNTGLTPCVSTSVFNQSKDFCVMVQIVPRVYHPEEVLDEYDYNRNP  
 POEV1 LVPGYNRWWACNTGLTPCVSTSVFNQSKDFCVMVQIVPRVYHPEEVLDEYDYNRNP  
 \*\*\*\*\* : \*\*\*\*\* : \*\*\*\*\* : \*\*\*\*\* : \*\*\*\*\* : \*\*\*\*\* : \*\*\*\*\* : \*

3/4

PERVA REPISLTLAVMLGLGVAAGVGTGTAALITGPQOLEKGLSNLHRIVTEDLQALEKSV SNLE  
POEVMSL REPISLTLAVMLGLGVAAGVGTGTAALVTGPQOLETGLSNLHRIVTEDLQALEKSV SNLE  
TSUKUBA REPISLTLAVMLGLGVAAGVGTGTAALVTGPQOLETGLSNLHRIVTEDLQALEKSV SNLE  
PERVB REPVSLTLAVMLGLGTAVGVGTGTAALITGPQOLEKGLGELHAAMTEDLRALKEESV SNLE  
POEV1 REPVSLTLAVMLGLGTAVGVGTGTAALITGPQOLEKGLGELHAAMTEDLRALKESV SNLE  
:.\*:\*\*\*\*\*. .\*\* \*\*\*\*\*:\*\*\*\*\*.\*\*\*:\*\* :\* :\*:\*\*\*\*\*

PERVA ESLSLSEVVLQNRRLDLLFLKEGGGLCVALKEECCFYVDHSGAIRDMSKLRERLERRR  
POEVMSL ESLSLSEVVLQNRRLDLLFLKEGGGLCVALKEECCFYVDHSGAIRDMSNKLRLERLEKRR  
TSUKUBA ESLSLSEVVLQNRRLDLLFLKEGGGLCVALKEECCFYVDHSGAIRDMSNKLRLERLEKRR  
PERVB ESLSLSEVVLQNRRLDLLFLREGGLCAALKEECCFYVDHSGAIRDMSKLRERLERRR  
POEV1 ESLSLSEVVLQNRRLDLLFLREGGLCAALKEECCFYVDHSGAIRDMSNKLRLKLERRR  
:\*\*\*\*\*:\*\*\*\*\*: \*\* \*\*\*\*\*:\*\*\*\*\*:\*\*\*\*\*.\*\*\*:\*\*:\*

PERVA REREADQGWFEWGFNRSPWMTTLLSALTGPLVLLLLLLTVGPCLINRFVAFVRERVS AVQ  
POEVMSL REKETQGWFEWGFNRSLWLATLLSALTGPLIVLLLLLLTVGPCIINKLIAFIRERIS AVQ  
TSUKUBA REKETQGWFEWGFNRSPWLATLLSALTGPLIVLLLLLLTVGPCIINKLIAFIRERIS AVQ  
PERVB REREADQGWFEWGFNRSPWMTTLLSALTGPLVLLLLLLTVGPCLINRFVAFVRERVS AVQ  
POEV1 REREADQGWFEWGFNRSPWMTTLLSALTGPLVLLLLLLTVGPCLINRFVAFVRERVS AVQ  
\*\*:\* \* \*\* :\*:\*\*\* \*:\*\*\*\*\*:\*\*\*\*\*:\*\*\*\*\*:\*\*\*\*\*:\*\*\*\*\*:\*\*\*\*\*:\*\*\*\*\*

PERVA IMVLRQQYQGLLSQGETDL  
POEVMSL IMVLRQQYQSPSSR-EAGR  
TSUKUBA IMVLRQQYQSPSSR-EAGR  
PERVB IMVLRQQYQGLLSQGETDL  
POEV1 IMVLRQQYQGLLSQGETDL  
\*\*\*\*\*. .: \*:

FIGURE 2

10/069082

4/4

PERVA	NNEEYCGNPQDFFCKQWSCITSNDGNWKWPVSQQDRVSYSFVNNPTSYNQFNyghgrwkd
POEVMSL	NNGKHCGNPRDFFCKQWNCVTSNDGYWKWPTSQQDRVSFSYVNTYTSSGQFNy-----LT
TSUKUBA	NNGKHCGNPRDFFCKQWNCVTSNDGYWKWPTSQQDRVSFSYVNTYTSSGQFNy-----LT
PERVB	EKEKYCGGSGESFCRRWSCVTSNDGDWKWPI SLQDRVKFSFVNSG--PGKYKVMK-----
POEV1	EKEKYCGGSGESFCRRWSCVTSNDGDWKWPI SLQDRVKFSFVNSG--PGKYKMMK-----
PERVA	wqqrqvqkdvrnkqisCHSLDL DYLKISFTE--KGKQENIQKWVNGISWGIVYYGGSGRKK
POEVMSL	W-----IRTGSPKCSPSDDL DYLKISFTE--KGKQENILKWVNGMSWGMVYYGGSGKQP
TSUKUBA	W-----IRTGSPKCSPSDDL DYLKISFTE--KGKQENILKWVNGMSWGMVYYGGSGKQP
PERVB	-----LYKDKSCSPSDDL DYLKISFTE--kgkqeniqkwngmsWGIVFYKYGGG-A
POEV1	-----LYKDKSCSPSDDL DYLKISFTErktgkyskvdkwy---elgnsFLLYGGG-A
PERVA	GSVLTIRLRIETQMEPPVAIGPNKGLAEQGPPIqeqrp-spnp sd-----yntt
POEVMSL	GSILTIRLKIN-QLEPPMAIGPNTVLTGQRPPTQ-----GPGPS-----SNIT
TSUKUBA	GSILTIRLKIN-QLEPPMAIGPntvltgqrpptq-----GPGPS-----SNIT
PERVB	GSTLTIRLRIETGTEPPVAVGPDKVLAEQGP PALEPPHNLVPVQLTSLRPDITQPPSNGT
POEV1	GSTLTIRLRIETGTEPPVAMGPDKVLAEQGP PALEPPHNLVPVQLTslrpditqppsnt
PERVA	SGSVPT-----EPNITIKTGAKLFSLIQGAFOALNSTTPEATSSCWLC LASGPPYYEGMA
POEVMSL	SGSDPT-----ESNSTTKMGAKLFSLIQGAFOALNSTTPEATSSCWLC LASGPPYYEGMA
TSUKUBA	SGSDPT-----ESSSTTKMGAKLFSLIQGAFOALNSTTPEATSSCWLC LALGPPYYEGMA
PERVB	TGLIPTNTPRNSPGVPVKTGQRLFSLIQGAFOAINSTD PDATSSCWLC LSSGPPYYEGMA
POEV1	TGLIPTNTPRNSPGVPVKTGQRLFSLIQGAFOAINSTD PDATSSCWLC LSSGPPYYEGMA

FIGURE 3



ATTORNEY DOCKET NO. 9013.43

**DECLARATION, POWER OF ATTORNEY AND PETITION**

As the below named inventor, I hereby declare:

my residence, post office address and citizenship are as stated below next to my name.

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled \_\_\_\_\_

RETROVIRUS ASSAY \_\_\_\_\_, the specification of which  
☐ is attached hereto.

☒ was filed on Feb. 15, 2002,

as Application Serial No. 10/069,082

and was amended on \_\_\_\_\_ (if applicable).

☒ was described and claimed in PCT International Application No. PCT/GB00/03159  
and as amended under PCT Article 19 on \_\_\_\_\_ (if any).

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose to the United States Patent & Trademark Office all information known to me to be material to patentability as defined in Title 37, Code of Federal Regulations, §1.56.

**PRIORITY CLAIM UNDER 35 USC § 119(a)-(d)**

I hereby claim foreign priority benefits under Title 35, United States Code, §119(a)-(d) or §365(b) of any foreign applications(s) for patent or inventor's certificate, or §365(a) of any PCT International Applications designating at least one country other than the U.S. listed below and have also identified below any foreign application for patent or inventor's certificate or of any PCT International Applications designating at least one country other than the U.S. having a filing date before that of the application on which priority is claimed:

☐ no such applications have been filed

☒ application(s) listed below:

[illegible]

9919604.0            United Kingdom            18 August 1999  
(Number)            (Country)            (Day/month/year filed)

(Number)	(Country)	(Day/month/year filed)	[ ]	[ ]
----------	-----------	------------------------	-----	-----

I hereby claim the benefit under Title 35, United States Code, §119(e) of any United States Provisional application listed below:

FILING DATE

I hereby claim the benefit under Title 35, United States Code, §120 of any United States application(s), or §365(c) of any PCT International Application(s) designating the U.S. listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States application in the manner provided by the first paragraph of Title 35, United States Code, §112, I acknowledge the duty to disclose to the U.S. Patent & Trademark Office all information known to me to be material to patentability as defined in Title 37, Code of Federal Regulations, §1.56 which became available between the filing date of the prior application and the national or PCT international filing date of this application:

(App. Serial No.)	(Filing date)	(Status) (patented, pending, abandoned)

[illegible]

**2018年12月26日**

(Filed More Than Twelve Months (Six Months for Design) Prior To This Application)

(Number)	(Country)	(Day/month/year filed)
----------	-----------	------------------------

(Number)	(Country)	(Day/month/year filed)
----------	-----------	------------------------

(Number)	(Country)	(Day/month/year filed)
----------	-----------	------------------------

POWER OF ATTORNEY

And I hereby appoint the practitioners associated with the Customer Number provided below as my attorneys, to prosecute this application and to transact all business in the United States Patent and Trademark Office connected therewith, and direct that all correspondence be addressed to that Customer Number:

Customer Number 20792

Send correspondence to: Kenneth D Sibley  
Myers Bigel Sibley & Sajovec  
Post Office Box 37428  
Raleigh, NC 27627

Direct telephone calls to: Kenneth D Sibley  
(919) 854 1400

Facsimile: (919) 854 1401

## DECLARATION

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Full name of sole or first inventor Daniel GALBRAITH

100  
Inventor's signature D. Galbraith

Date 3/10/02 Citizenship British

Residence Glasgow, United Kingdom GBX

Post Office Address 513 Alexandra Parade, Glasgow, G31 3EW, United Kingdom

Full name of second, joint inventor, if any Helena KELLY

200  
Inventor's signature Helena T. Kelly

Date 4<sup>th</sup> October 2002 Citizenship British

Residence Glasgow, United Kingdom GBX

Post Office Address Flat 1/2, 19 Kelvindale Gardens, Glasgow, G20 8DW, United Kingdom

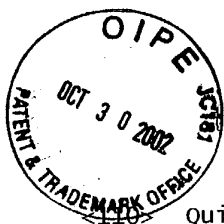
Full name of third, joint inventor, if any Kenneth SMITH

300  
Inventor's signature Kenneth Smith

Date 7<sup>th</sup> October 2002 Citizenship British

Residence Glasgow, United Kingdom GBX

Post Office Address 5 Capelrig Lane, Newton Mearns, Glasgow, G77 6XZ, United Kingdom



Rec'd PCT/PTO 30 OCT 2002  
10/069082

SEQUENCE LISTING

Quip Technology Limited

<120> Retrovirus Assay

<130> P10890US

<140> US 10/069,082

<141> 2000-08-16

<150> GB 9919604.0

<151> 1999-08-18

<150> PCT/GB00/03159

<151> 2000-08-16

<160> 19

<170> PatentIn version 3.1

<210> 1

<211> 524

<212> PRT

<213> porcine endogenous retrovirus

<400> 1

Met Gly Gln Thr Val Thr Thr Pro Leu Ser Leu Thr Leu Asp His Trp  
1 5 10 15

Thr Glu Val Arg Ser Arg Ala His Asn Leu Ser Val Gln Val Lys Lys  
20 25 30

Gly Pro Trp Gln Thr Phe Cys Ala Ser Glu Trp Pro Thr Phe Asp Val  
35 40 45

Gly Trp Pro Ser Glu Gly Thr Phe Asn Ser Glu Ile Ile Leu Ala Val  
50 55 60

Lys Ala Ile Ile Phe Gln Thr Gly Pro Gly Ser His Pro Asp Gln Glu  
 65 70 75 80  
 Pro Tyr Ile Leu Thr Trp Gln Asp Leu Ala Glu Asp Pro Pro Pro Trp  
 85 90 95  
 Val Lys Pro Trp Leu Asn Lys Pro Arg Lys Pro Gly Pro Arg Ile Leu  
 100 105 110  
 Ala Leu Gly Glu Lys Asn Lys His Ser Ala Glu Lys Val Glu Pro Ser  
 115 120 125  
 Ser Ser Tyr Leu Pro Arg Asp Arg Gly Ala Ala Asp Leu Ala Gly Thr  
 130 135 140  
 Pro Thr Cys Ser Pro Thr Pro Leu Ser Ser Thr Gly Cys Cys Glu Gly  
 145 150 155 160  
 Thr Ser Ala Pro Pro Gly Ala Pro Val Val Glu Gly Pro Ala Ala Gly  
 165 170 175  
 Thr Arg Ser Arg Arg Gly Ala Thr Pro Glu Arg Thr Asp Glu Ile Ala  
 180 185 190  
 Ile Leu Pro Leu Arg Thr Tyr Gly Pro Pro Met Pro Gly Gly Gln Leu  
 195 200 205  
 Gln Pro Leu Gln Tyr Trp Pro Phe Ser Ser Ala Asp Leu Tyr Asn Trp  
 210 215 220  
 Lys Thr Asn His Pro Pro Phe Ser Glu Asp Pro Gln Arg Leu Thr Gly  
 225 230 235 240  
 Leu Val Glu Ser Leu Met Phe Ser His Gln Pro Thr Trp Asp Asp Cys  
 245 250 255  
 Gln Gln Leu Leu Gln Thr Leu Phe Thr Thr Glu Glu Arg Glu Arg Ile  
 260 265 270  
 Leu Leu Glu Ala Arg Lys Asn Val Pro Gly Ala Asp Gly Arg Pro Thr  
 275 280 285  
 Gln Leu Gln Asn Glu Ile Asp Met Gly Phe Pro Leu Thr Arg Pro Gly  
 290 295 300  
 Trp Asp Tyr Asn Thr Ala Glu Gly Arg Glu Ser Leu Lys Ile Tyr Arg  
 305 310 315 320  
 Gln Ala Leu Val Ala Gly Leu Arg Gly Ala Ser Arg Arg Pro Thr Asn  
 325 330 335  
 Leu Ala Lys Val Arg Glu Val Met Gln Gly Pro Asn Glu Pro Pro Ser  
 340 345 350

1971	1972	1973	1974	1975	1976	1977	1978	1979	1980	1981	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031	2032	2033	2034	2035	2036	2037	2038	2039	2040	2041	2042	2043	2044	2045	2046	2047	2048	2049	2050	2051	2052	2053	2054	2055	2056	2057	2058	2059	2060	2061	2062	2063	2064	2065	2066	2067	2068	2069	2070	2071	2072	2073	2074	2075	2076	2077	2078	2079	2080	2081	2082	2083	2084	2085	2086	2087	2088	2089	2090	2091	2092	2093	2094	2095	2096	2097	2098	2099	2100	2101	2102	2103	2104	2105	2106	2107	2108	2109	2110	2111	2112	2113	2114	2115	2116	2117	2118	2119	2120	2121	2122	2123	2124	2125	2126	2127	2128	2129	2130	2131	2132	2133	2134	2135	2136	2137	2138	2139	2140	2141	2142	2143	2144	2145	2146	2147	2148	2149	2150	2151	2152	2153	2154	2155	2156	2157	2158	2159	2160	2161	2162	2163	2164	2165	2166	2167	2168	2169	2170	2171	2172	2173	2174	2175	2176	2177	2178	2179	2180	2181	2182	2183	2184	2185	2186	2187	2188	2189	2190	2191	2192	2193	2194	2195	2196	2197	2198	2199	2200	2201	2202	2203	2204	2205	2206	2207	2208	2209	2210	2211	2212	2213	2214	2215	2216	2217	2218	2219	2220	2221	2222	2223	2224	2225	2226	2227	2228	2229	2230	2231	2232	2233	2234	2235	2236	2237	2238	2239	2240	2241	2242	2243	2244	2245	2246	2247	2248	2249	2250	2251	2252	2253	2254	2255	2256	2257	2258	2259	2260	2261	2262	2263	2264	2265	2266	2267	2268	2269	2270	2271	2272	2273	2274	2275	2276	2277	2278	2279	2280	2281	2282	2283	2284	2285	2286	2287	2288	2289	2290	2291	2292	2293	2294	2295	2296	2297	2298	2299	2300	2301	2302	2303	2304	2305	2306	2307	2308	2309	2310	2311	2312	2313	2314	2315	2316	2317	2318	2319	2320	2321	2322	2323	2324	2325	2326	2327	2328	2329	2330	2331	2332	2333	2334	2335	2336	2337	2338	2339	2340	2341	2342	2343	2344	2345	2346	2347	2348	2349	2350	2351	2352	2353	2354	2355	2356	2357	2358	2359	2360	2361	2362	2363	2364	2365	2366	2367	2368	2369	2370	2371	2372	2373	2374	2375	2376	2377	2378	2379	2380	2381	2382	2383	2384	2385	2386	2387	2388	2389	2390	2391	2392	2393	2394	2395	2396	2397	2398	2399	2400	2401	2402	2403	2404	2405	2406	2407	2408	2409	2410	2411	2412	2413	2414	2415	2416	2417	2418	2419	2420	2421	2422	2423	2424
------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------

Ser Pro Asn Ser His Lys Pro Leu Ser Leu Thr Trp Leu Leu Thr Asp  
50 55 60

Ser Gly Thr Gly Ile Asn Ile Asn Ser Thr Gln Gly Glu Ala Pro Leu  
65 70 75 80

Gly Thr Trp Trp Pro Glu Leu Tyr Val Cys Leu Arg Ser Val Ile Pro  
85 90 95

Gly Leu Asn Asp Gln Ala Thr Pro Pro Asp Val Leu Arg Ala Tyr Gly  
100 105 110

Phe Tyr Val Cys Pro Gly Pro Pro Asn Asn Glu Glu Tyr Cys Gly Asn  
115 120 125

Pro Gln Asp Phe Phe Cys Lys Gln Trp Ser Cys Ile Thr Ser Asn Asp  
130 135 140

Gly Asn Trp Lys Trp Pro Val Ser Gln Gln Asp Arg Val Ser Tyr Ser  
145 150 155 160

Phe Val Asn Asn Pro Thr Ser Tyr Asn Gln Phe Asn Tyr Gly His Gly  
165 170 175

Arg Trp Lys Asp Trp Gln Gln Arg Val Gln Lys Asp Val Arg Asn Lys  
180 185 190

Gln Ile Ser Cys His Ser Leu Asp Leu Asp Tyr Leu Lys Ile Ser Phe  
195 200 205

Thr Glu Lys Gly Lys Gln Glu Asn Ile Gln Lys Trp Val Asn Gly Ile  
210 215 220

Ser Trp Gly Ile Val Tyr Tyr Gly Gly Ser Gly Arg Lys Lys Gly Ser  
225 230 235 240

Val Leu Thr Ile Arg Leu Arg Ile Glu Thr Gln Met Glu Pro Pro Val  
245 250 255

Ala Ile Gly Pro Asn Lys Gly Leu Ala Glu Gln Gly Pro Pro Ile Gln  
260 265 270

Glu Gln Arg Pro Ser Pro Asn Pro Ser Asp Tyr Asn Thr Thr Ser Gly  
275 280 285

Ser Val Pro Thr Glu Pro Asn Ile Thr Ile Lys Thr Gly Ala Lys Leu  
290 295 300

Phe Ser Leu Ile Gln Gly Ala Phe Gln Ala Leu Asn Ser Thr Thr Pro  
305 310 315 320

Glu Ala Thr Ser Ser Cys Trp Leu Cys Leu Ala Ser Gly Pro Pro Tyr  
325 330 335

Tyr Glu Gly Met Ala Arg Gly Gly Lys Phe Asn Val Thr Lys Glu His  
 340 345 350  
 Arg Asp Gln Cys Thr Trp Gly Ser Gln Asn Lys Leu Thr Leu Thr Glu  
 355 360 365  
 Val Ser Gly Lys Gly Thr Cys Ile Gly Met Val Pro Pro Ser His Gln  
 370 375 380  
 His Leu Cys Asn His Thr Glu Ala Phe Asn Arg Thr Ser Glu Ser Gln  
 385 390 395 400  
 Tyr Leu Val Pro Gly Tyr Asp Arg Trp Trp Ala Cys Asn Thr Gly Leu  
 405 410 415  
 Thr Pro Cys Val Ser Thr Leu Val Phe Asn Gln Thr Lys Asp Phe Cys  
 420 425 430  
 Val Met Val Gln Ile Val Pro Arg Val Tyr Tyr Tyr Pro Glu Lys Ala  
 435 440 445  
 Val Leu Asp Glu Tyr Asp Tyr Arg Tyr Asn Arg Pro Lys Arg Glu Pro  
 450 455 460  
 Ile Ser Leu Thr Leu Ala Val Met Leu Gly Leu Gly Val Ala Ala Gly  
 465 470 475 480  
 Val Gly Thr Gly Thr Ala Ala Leu Ile Thr Gly Pro Gln Gln Leu Glu  
 485 490 495  
 Lys Gly Leu Ser Asn Leu His Arg Ile Val Thr Glu Asp Leu Gln Ala  
 500 505 510  
 Leu Glu Lys Ser Val Ser Asn Leu Glu Glu Ser Leu Thr Ser Leu Ser  
 515 520 525  
 Glu Val Val Leu Gln Asn Arg Arg Gly Leu Asp Leu Leu Phe Leu Lys  
 530 535 540  
 Glu Gly Gly Leu Cys Val Ala Leu Lys Glu Glu Cys Cys Phe Tyr Val  
 545 550 555 560  
 Asp His Ser Gly Ala Ile Arg Asp Ser Met Ser Lys Leu Arg Glu Arg  
 565 570 575  
 Leu Glu Arg Arg Arg Arg Glu Arg Glu Ala Asp Gln Gly Trp Phe Glu  
 580 585 590  
 Gly Trp Phe Asn Arg Ser Pro Trp Met Thr Thr Leu Leu Ser Ala Leu  
 595 600 605

Thr Gly Pro Leu Val Val Leu Leu Leu Leu Thr Val Gly Pro Cys  
 610 615 620

Leu Ile Asn Arg Phe Val Ala Phe Val Arg Glu Arg Val Ser Ala Val  
 625 630 635 640

Gln Ile Met Val Leu Arg Gln Gln Tyr Gln Gly Leu Leu Ser Gln Gly  
 645 650 655

Glu Thr Asp Leu  
 660

<210> 3

<211> 638

<212> PRT

<213> porcine endogenous retrovirus Type PERV MSL

<400> 3

Met His Pro Thr Leu Asn Arg Arg His Leu Pro Ile Arg Gly Gly Lys  
 1 5 10 15

Pro Lys Arg Leu Lys Ile Pro Leu Ser Phe Ala Ser Ile Ala Trp Phe  
 20 25 30

Leu Thr Leu Ser Ile Thr Ser Gln Thr Asn Gly Met Arg Ile Gly Asp  
 35 40 45

Ser Leu Asn Ser His Lys Pro Leu Ser Leu Thr Trp Leu Ile Thr Asp  
 50 55 60

Ser Gly Thr Gly Ile Asn Ile Asn Asn Thr Gln Gly Glu Ala Pro Leu  
 65 70 75 80

Gly Thr Trp Trp Pro Asp Leu Tyr Val Cys Leu Arg Ser Val Ile Pro  
 85 90 95

Ser Leu Thr Ser Pro Pro Asp Ile Leu His Ala His Gly Phe Tyr Val  
 100 105 110

Cys Pro Gly Pro Pro Asn Asn Gly Lys His Cys Gly Asn Pro Arg Asp  
 115 120 125

Phe Phe Cys Lys Gln Trp Asn Cys Val Thr Ser Asn Asp Gly Tyr Trp  
 130 135 140

Lys Trp Pro Thr Ser Gln Gln Asp Arg Val Ser Phe Ser Tyr Val Asn  
 145 150 155 160

Thr Tyr Thr Ser Ser Gly Gln Phe Asn Tyr Leu Thr Trp Ile Arg Thr  
 165 170 175

Gly Ser Pro Lys Cys Ser Pro Ser Asp Leu Asp Tyr Leu Lys Ile Ser  
180 185 190

Phe Thr Glu Lys Gly Lys Gln Glu Asn Ile Leu Lys Trp Val Asn Gly  
195 200 205

Met Ser Trp Gly Met Val Tyr Tyr Gly Gly Ser Gly Lys Gln Pro Gly  
210 215 220

Ser Ile Leu Thr Ile Arg Leu Lys Ile Asn Gln Leu Glu Pro Pro Met  
225 230 235 240

Ala Ile Gly Pro Asn Thr Val Leu Thr Gly Gln Arg Pro Pro Thr Gln  
245 250 255

Gly Pro Gly Pro Ser Ser Asn Ile Thr Ser Gly Ser Asp Pro Thr Glu  
260 265 270

Ser Asn Ser Thr Thr Lys Met Gly Ala Lys Leu Phe Ser Leu Ile Gln  
275 280 285

Gly Ala Phe Gln Ala Leu Asn Ser Thr Thr Pro Glu Ala Thr Ser Ser  
290 295 300

Cys Trp Leu Cys Leu Ala Ser Gly Pro Pro Tyr Tyr Glu Gly Met Ala  
305 310 315 320

Arg Arg Gly Lys Phe Asn Val Thr Lys Glu His Arg Asp Gln Cys Thr  
325 330 335

Trp Gly Ser Gln Asn Lys Leu Thr Leu Thr Glu Val Ser Gly Lys Gly  
340 345 350

Thr Cys Ile Gly Lys Val Pro Pro Ser His Gln His Leu Cys Asn His  
355 360 365

Thr Glu Ala Phe Asn Gln Thr Ser Glu Ser Gln Tyr Leu Val Pro Gly  
370 375 380

Tyr Asp Arg Trp Trp Ala Cys Asn Thr Gly Leu Thr Pro Cys Val Ser  
385 390 395 400

Thr Leu Val Phe Asn Gln Thr Lys Asp Phe Cys Ile Met Val Gln Ile  
405 410 415

Val Pro Arg Val Tyr Tyr Tyr Pro Glu Lys Ala Ile Leu Asp Glu Tyr  
420 425 430

Asp Tyr Arg Asn His Arg Gln Lys Arg Glu Pro Ile Ser Leu Thr Leu  
435 440 445

Ala Val Met Leu Gly Leu Gly Val Ala Ala Gly Val Gly Thr Gly Thr  
450 455 460

Ala Ala Leu Val Thr Gly Pro Gln Gln Leu Glu Thr Gly Leu Ser Asn  
465 470 475 480

Leu His Arg Ile Val Thr Glu Asp Leu Gln Ala Leu Glu Lys Ser Val  
485 490 495

Ser Asn Leu Glu Glu Ser Leu Thr Ser Leu Ser Glu Val Val Leu Gln  
500 505 510

Asn Arg Arg Gly Leu Asp Leu Leu Phe Leu Lys Glu Gly Gly Leu Cys  
515 520 525

Val Ala Leu Lys Glu Glu Cys Cys Phe Tyr Val Asp His Ser Gly Ala  
530 535 540

Ile Arg Asp Ser Met Asn Lys Leu Arg Glu Arg Leu Glu Lys Arg Arg  
545 550 555 560

Arg Glu Lys Glu Thr Thr Gln Gly Trp Phe Glu Gly Trp Phe Asn Arg  
565 570 575

Ser Leu Trp Leu Ala Thr Leu Leu Ser Ala Leu Thr Gly Pro Leu Ile  
580 585 590

Val Leu Leu Leu Leu Leu Thr Val Gly Pro Cys Ile Ile Asn Lys Leu  
595 600 605

Ile Ala Phe Ile Arg Glu Arg Ile Ser Ala Val Gln Ile Met Val Leu  
610 615 620

Arg Gln Gln Tyr Gln Ser Pro Ser Ser Arg Glu Ala Gly Arg  
625 630 635

<210> 4

<211> 638

<212> PRT

<213> porcine endogenous retrovirus Type Tsukuba

<400> 4

Met His Pro Thr Leu Ser Arg Arg His Leu Pro Ile Arg Gly Gly Lys  
1 5 10 15

Pro Lys Arg Leu Lys Ile Pro Leu Ser Phe Ala Ser Ile Ala Trp Phe  
20 25 30

Leu Thr Leu Ser Ile Thr Ser Gln Thr Asn Gly Met Arg Ile Gly Asp  
35 40 45

Ser Leu Asn Ser His Lys Pro Leu Ser Leu Thr Trp Leu Ile Thr Asp  
50 55 60

Ser Gly Thr Gly Ile Asn Ile Asn Asn Thr Gln Gly Glu Ala Pro Leu  
65 70 75 80

Gly Thr Trp Trp Pro Asp Leu Tyr Val Cys Leu Arg Ser Val Ile Pro  
85 90 95

Ser Leu Thr Ser Pro Pro Asp Ile Leu His Ala His Gly Phe Tyr Val  
100 105 110

Cys Pro Gly Pro Pro Asn Asn Gly Lys His Cys Gly Asn Pro Arg Asp  
115 120 125

Phe Phe Cys Lys Gln Trp Asn Cys Val Thr Ser Asn Asp Gly Tyr Trp  
130 135 140

Lys Trp Pro Thr Ser Gln Gln Asp Arg Val Ser Phe Ser Tyr Val Asn  
145 150 155 160

Thr Tyr Thr Ser Ser Gly Gln Phe Asn Tyr Leu Thr Trp Ile Arg Thr  
165 170 175

Gly Ser Pro Lys Cys Ser Pro Ser Asp Leu Asp Tyr Leu Lys Ile Ser  
180 185 190

Phe Thr Glu Lys Gly Lys Gln Glu Asn Ile Leu Lys Trp Val Asn Gly  
195 200 205

Met Ser Trp Gly Met val Tyr Tyr Gly Gly Ser Gly Lys Gln Pro Gly  
210 215 220

Ser Ile Leu Thr Ile Arg Leu Lys Ile Asn Gln Leu Glu Pro Pro Met  
225 230 235 240

Ala Ile Gly Pro Asn Thr Val Leu Thr Gly Gln Arg Pro Pro Thr Gln  
245 250 255

Gly Pro Gly Pro Ser Ser Asn Ile Thr Ser Gly Ser Asp Pro Thr Glu  
260 265 270

Ser Ser Ser Thr Thr Lys Met Gly Ala Lys Leu Phe Ser Leu Ile Gln  
275 280 285

Gly Ala Phe Gln Ala Leu Asn Ser Thr Thr Pro Glu Ala Thr Ser Ser  
290 295 300

Cys Trp Leu Cys Leu Ala Leu Gly Pro Pro Tyr Tyr Glu Gly Met Ala  
305 310 315 320

Arg Arg Gly Lys Phe Asn Val Thr Lys Glu His Arg Asp Gln Cys Thr  
325 330 335

Trp Gly Ser Gln Asn Lys Leu Thr Leu Thr Glu Val Ser Gly Lys Gly  
340 345 350

Thr Cys Ile Gly Lys Val Pro Pro Ser His Gln His Leu Cys Asn His  
355 360 365

Thr Glu Ala Phe Asn Gln Thr Ser Glu Ser Gln Tyr Leu Val Pro Gly  
370 375 380

Tyr Asp Arg Trp Trp Ala Cys Asn Thr Gly Leu Thr Pro Cys Val Ser  
385 390 395 400

Thr Leu Val Phe Asn Gln Thr Lys Asp Phe Cys Ile Met Val Gln Ile  
405 410 415

Val Pro Arg Val Tyr Tyr Tyr Pro Glu Lys Ala Ile Leu Asp Glu Tyr  
420 425 430

Asp Tyr Arg Asn His Arg Gln Lys Arg Glu Pro Ile Ser Leu Thr Leu  
435 440 445

Ala Val Met Leu Gly Leu Gly Val Ala Ala Gly Val Gly Thr Gly Thr  
450 455 460

Ala Ala Leu Val Thr Gly Pro Gln Gln Leu Glu Thr Gly Leu Ser Asn  
465 470 475 480

Leu His Arg Ile Val Thr Glu Asp Leu Gln Ala Leu Glu Lys Ser Val  
485 490 495

Ser Asn Leu Glu Glu Ser Leu Thr Ser Leu Ser Glu Val Val Leu Gln  
500 505 510

Asn Arg Arg Gly Leu Asp Leu Leu Phe Leu Lys Glu Gly Gly Leu Cys  
515 520 525

Val Ala Leu Lys Glu Glu Cys Cys Phe Tyr Val Asp His Ser Gly Ala  
530 535 540

Ile Arg Asp Ser Met Asn Lys Leu Arg Glu Arg Leu Glu Lys Arg Arg  
545 550 555 560

Arg Glu Lys Glu Thr Thr Gln Gly Trp Phe Glu Gly Trp Phe Asn Arg  
565 570 575

Ser Pro Trp Leu Ala Thr Leu Leu Ser Ala Leu Thr Gly Pro Leu Ile  
580 585 590

Val Leu Leu Leu Leu Leu Thr Val Gly Pro Cys Ile Ile Asn Lys Leu  
595 600 605

Ile Ala Phe Ile Arg Glu Arg Ile Ser Ala Val Gln Ile Met Val Leu  
610 615 620

Arg Gln Gln Tyr Gln Ser Pro Ser Ser Arg Glu Ala Gly Arg  
625 630 635

<210> 5

<211> 657

<212> PRT

<213> porcine endogenous retrovirus Type PERV B

<400> 5

Met His Pro Thr Leu Ser Trp Arg His Leu Pro Thr Arg Gly Gly Glu  
1 5 10 15

Pro Lys Arg Leu Arg Ile Pro Leu Ser Phe Ala Ser Ile Ala Trp Phe  
20 25 30

Leu Thr Leu Thr Ile Thr Pro Gln Ala Ser Ser Lys Arg Leu Ile Asp  
35 40 45

Ser Ser Asn Pro His Arg Pro Leu Ser Leu Thr Trp Leu Ile Ile Asp  
50 55 60

Pro Asp Thr Gly Val Thr Val Asn Ser Thr Arg Gly Val Ala Pro Arg  
65 70 75 80

Gly Thr Trp Trp Pro Glu Leu His Phe Cys Leu Arg Leu Ile Asn Pro  
85 90 95

Ala Val Lys Ser Thr Pro Pro Asn Leu Val Arg Ser Tyr Gly Phe Tyr  
100 105 110

Cys Cys Pro Gly Thr Glu Lys Glu Lys Tyr Cys Gly Gly Ser Gly Glu  
115 120 125

Ser Phe Cys Arg Arg Trp Ser Cys Val Thr Ser Asn Asp Gly Asp Trp  
130 135 140

Lys Trp Pro Ile Ser Leu Gln Asp Arg Val Lys Phe Ser Phe Val Asn  
145 150 155 160

Ser Gly Pro Gly Lys Tyr Lys Val Met Lys Leu Tyr Lys Asp Lys Ser  
165 170 175

Cys Ser Pro Ser Asp Leu Asp Tyr Leu Lys Ile Ser Phe Thr Glu Lys  
180 185 190

Gly Lys Gln Glu Asn Ile Gln Lys Trp Ile Asn Gly Met Ser Trp Gly  
195 200 205

Ile Val Phe Tyr Lys Tyr Gly Gly Gly Ala Gly Ser Thr Leu Thr Ile  
210 215 220

Arg Leu Arg Ile Glu Thr Gly Thr Glu Pro Pro Val Ala Val Gly Pro  
225 230 235 240

Asp Lys Val Leu Ala Glu Gln Gly Pro Pro Ala Leu Glu Pro Pro His  
245 250 255

Asn Leu Pro Val Pro Gln Leu Thr Ser Leu Arg Pro Asp Ile Thr Gln  
260 265 270

Pro Pro Ser Asn Gly Thr Thr Gly Leu Ile Pro Thr Asn Thr Pro Arg  
275 280 285

Asn Ser Pro Gly Val Pro Val Lys Thr Gly Gln Arg Leu Phe Ser Leu  
290 295 300

Ile Gln Gly Ala Phe Gln Ala Ile Asn Ser Thr Asp Pro Asp Ala Thr  
305 310 315 320

Ser Ser Cys Trp Leu Cys Leu Ser Ser Gly Pro Pro Tyr Tyr Glu Gly  
325 330 335

Met Ala Lys Glu Gly Lys Phe Asn Val Thr Lys Glu His Arg Asn Gln  
340 345 350

Cys Thr Trp Gly Ser Arg Asn Lys Leu Thr Leu Thr Glu Val Ser Gly  
355 360 365

Lys Gly Thr Cys Ile Gly Lys Ala Pro Pro Ser His Gln His Leu Cys  
370 375 380

Tyr Ser Thr Val Val Tyr Glu Gln Ala Ser Glu Asn Gln Tyr Leu Val  
385 390 395 400

Pro Gly Tyr Asn Arg Trp Trp Ala Cys Asn Thr Gly Leu Thr Pro Cys  
405 410 415

Val Ser Thr Ser Val Phe Asn Gln Ser Lys Asp Phe Cys Val Met Val  
420 425 430

Gln Ile Val Pro Arg Val Tyr Tyr His Pro Glu Glu Val Val Leu Asp  
435 440 445

Glu Tyr Asp Tyr Arg Tyr Asn Arg Pro Lys Arg Glu Pro Val Ser Leu  
450 455 460

Thr Leu Ala Val Met Leu Gly Leu Gly Thr Ala Val Gly Val Gly Thr  
465 470 475 480

Gly Thr Ala Ala Leu Ile Thr Gly Pro Gln Gln Leu Glu Lys Gly Leu  
485 490 495

Gly Glu Leu His Ala Ala Met Thr Glu Asp Leu Arg Ala Leu Glu Glu  
500 505 510

Ser Val Ser Asn Leu Glu Glu Ser Leu Thr Ser Leu Ser Glu Val Val  
515 520 525

Leu Gln Asn Arg Arg Gly Leu Asp Leu Leu Phe Leu Arg Glu Gly Gly  
530 535 540

Leu Cys Ala Ala Leu Lys Glu Glu Cys Cys Phe Tyr Val Asp His Ser  
545 550 555 560

Gly Ala Ile Arg Asp Ser Met Ser Lys Leu Arg Glu Arg Leu Glu Arg  
565 570 575

Arg Arg Arg Glu Arg Glu Ala Asp Gln Gly Trp Phe Glu Gly Trp Phe  
580 585 590

Asn Arg Ser Pro Trp Met Thr Thr Leu Leu Ser Ala Leu Thr Gly Pro  
595 600 605

Leu Val Val Leu Leu Leu Leu Leu Thr Val Gly Pro Cys Leu Ile Asn  
610 615 620

Arg Phe Val Ala Phe Val Arg Glu Arg Val Ser Ala Val Gln Ile Met  
625 630 635 640

Val Leu Arg Gln Gln Tyr Gln Gly Leu Leu Ser Gln Gly Glu Thr Asp  
645 650 655

Leu

<210> 6

<211> 656

<212> PRT

<213> porcine endogenous retrovirus Type PoEV1

<400> 6

Met His Pro Thr Leu Ser Arg Arg His Leu Pro Thr Arg Gly Gly Glu  
1 5 10 15

Pro Lys Arg Leu Arg Ile Pro Leu Ser Phe Ala Ser Ile Ala Trp Phe  
20 25 30

**FILED**      **FILED**

Leu	Thr	Leu	Thr	Ile	Thr	Pro	Gln	Ala	Ser	Ser	Lys	Arg	Leu	Ile	Asp
		35					40				45				
Ser	Ser	Asn	Pro	His	Arg	Pro	Leu	Ser	Leu	Thr	Trp	Leu	Ile	Ile	Asp
	50					55					60				
Pro	Asp	Thr	Gly	Val	Thr	Val	Asn	Ser	Thr	Arg	Gly	Val	Ala	Pro	Arg
65					70					75					80
Gly	Thr	Trp	Trp	Pro	Glu	Leu	His	Phe	Cys	Leu	Arg	Leu	Ile	Asn	Pro
				85					90					95	
Ala	Val	Lys	Ser	Thr	Pro	Pro	Asn	Leu	Val	Arg	Ser	Tyr	Gly	Phe	Tyr
			100					105					110		
Cys	Cys	Pro	Gly	Thr	Glu	Lys	Glu	Lys	Tyr	Cys	Gly	Gly	Ser	Gly	Glu
		115					120					125			
Ser	Phe	Cys	Arg	Arg	Trp	Ser	Cys	Val	Thr	Ser	Asn	Asp	Gly	Asp	Trp
	130					135					140				
Lys	Trp	Pro	Ile	Ser	Leu	Gln	Asp	Arg	Val	Lys	Phe	Ser	Phe	Val	Asn
145					150					155					160
Ser	Gly	Pro	Gly	Lys	Tyr	Lys	Met	Met	Lys	Leu	Tyr	Lys	Asp	Lys	Ser
				165					170					175	
Cys	Ser	Pro	Ser	Asp	Leu	Asp	Tyr	Leu	Lys	Ile	Ser	Phe	Thr	Glu	Arg
			180					185					190		
Lys	Thr	Gly	Lys	Tyr	Ser	Lys	Val	Asp	Lys	Trp	Tyr	Glu	Leu	Gly	Asn
		195					200					205			
Ser	Phe	Leu	Leu	Tyr	Gly	Gly	Gly	Ala	Gly	Ser	Thr	Leu	Thr	Ile	Arg
	210					215					220				
Leu	Arg	Ile	Glu	Thr	Gly	Thr	Glu	Pro	Pro	Val	Ala	Met	Gly	Pro	Asp
225					230					235					240
Lys	Val	Leu	Ala	Glu	Gln	Gly	Pro	Pro	Ala	Leu	Glu	Pro	Pro	His	Asn
				245					250					255	
Leu	Pro	Val	Pro	Gln	Leu	Thr	Ser	Leu	Arg	Pro	Asp	Ile	Thr	Gln	Pro
			260					265					270		
Pro	Ser	Asn	Ser	Thr	Thr	Gly	Leu	Ile	Pro	Thr	Asn	Thr	Pro	Arg	Asn
		275					280					285			
Ser	Pro	Gly	Val	Pro	Val	Lys	Thr	Gly	Gln	Arg	Leu	Phe	Ser	Leu	Ile
	290					295					300				
Gln	Gly	Ala	Phe	Gln	Ala	Ile	Asn	Ser	Thr	Asp	Pro	Asp	Ala	Thr	Ser
305					310					315					320

Ser Cys Trp Leu Cys<sub>325</sub> Leu Ser Ser Gly Pro<sub>330</sub> Pro Tyr Tyr Glu Gly<sub>335</sub> Met

Ala Lys Glu Arg<sub>340</sub> Lys Phe Asn Val Thr<sub>345</sub> Lys Glu His Arg Asn<sub>350</sub> Gln Cys

Thr Trp Gly<sub>355</sub> Ser Arg Asn Lys<sub>360</sub> Leu Thr Leu Thr Glu Val<sub>365</sub> Ser Gly Lys

Gly Thr<sub>370</sub> Cys Ile Gly Lys Ala<sub>375</sub> Pro Pro Ser His Gln<sub>380</sub> His Leu Cys Tyr

Ser Thr Val Val Tyr Glu<sub>390</sub> Gln Ala Ser Glu Asn<sub>395</sub> Gln Tyr Leu Val Pro<sub>400</sub>

Gly Tyr Asn Arg Trp<sub>405</sub> Trp Ala Cys Asn Thr<sub>410</sub> Gly Leu Thr Pro Cys<sub>415</sub> Val

Ser Thr Ser Val<sub>420</sub> Phe Asn Gln Ser Lys<sub>425</sub> Asp Phe Cys Val Met<sub>430</sub> Val Gln

Ile Val Pro Arg Val Tyr Tyr His<sub>440</sub> Pro Glu Glu Val Val<sub>445</sub> Leu Asp Glu

Tyr Asp Tyr Arg Tyr Asn Arg<sub>455</sub> Pro Lys Arg Glu Pro<sub>460</sub> Val Ser Leu Thr

Leu Ala Val Met Leu Gly<sub>470</sub> Leu Gly Thr Ala Val<sub>475</sub> Gly Val Gly Thr Gly<sub>480</sub>

Thr Ala Ala Leu Ile<sub>485</sub> Thr Gly Pro Gln Gln<sub>490</sub> Leu Glu Lys Gly Leu Gly<sub>495</sub>

Glu Leu His Ala<sub>500</sub> Ala Met Thr Glu Asp<sub>505</sub> Leu Arg Ala Leu Lys<sub>510</sub> Glu Ser

Val Ser Asn Leu Glu Glu Ser Leu Thr Ser Leu Ser Glu<sub>525</sub> Val Val Leu

Gln Asn Arg Arg Gly Leu Asp<sub>535</sub> Leu Leu Phe Leu Arg<sub>540</sub> Glu Gly Gly Leu

Cys Ala Ala Leu Lys Glu<sub>550</sub> Glu Cys Cys Phe Tyr<sub>555</sub> Val Asp His Ser Gly<sub>560</sub>

Ala Ile Arg Asp Ser Met Asn Lys Leu Arg<sub>570</sub> Lys Lys Leu Glu Arg<sub>575</sub> Arg

Arg Arg Glu Arg<sub>580</sub> Glu Ala Asp Gln Gly<sub>585</sub> Trp Phe Glu Gly Trp Phe Asn<sub>590</sub>

Arg Ser Pro Trp Met Thr Thr Leu Leu Ser Ala Leu Thr Gly Pro Leu  
595 600 605

Val Val Leu Leu Leu Leu Leu Thr Val Gly Pro Cys Leu Ile Asn Arg  
610 615 620

Phe Val Ala Phe Val Arg Glu Arg Val Ser Ala Val Gln Ile Met Val  
625 630 635 640

Leu Arg Gln Gln Tyr Gln Gly Leu Leu Ser Gln Gly Glu Thr Asp Leu  
645 650 655

<210> 7

<211> 221

<212> PRT

<213> porcine endogenous retrovirus Type PERV A

<400> 7

Asn Asn Glu Glu Tyr Cys Gly Asn Pro Gln Asp Phe Phe Cys Lys Gln  
1 5 10 15

Trp Ser Cys Ile Thr Ser Asn Asp Gly Asn Trp Lys Trp Pro Val Ser  
20 25 30

Gln Gln Asp Arg Val Ser Tyr Ser Phe Val Asn Asn Pro Thr Ser Tyr  
35 40 45

Asn Gln Phe Asn Tyr Gly His Gly Arg Trp Lys Asp Trp Gln Gln Arg  
50 55 60

Val Gln Lys Asp Val Arg Asn Lys Gln Ile Ser Cys His Ser Leu Asp  
65 70 75 80

Leu Asp Tyr Leu Lys Ile Ser Phe Thr Glu Lys Gly Lys Gln Glu Asn  
85 90 95

Ile Gln Lys Trp Val Asn Gly Ile Ser Trp Gly Ile Val Tyr Tyr Gly  
100 105 110

Gly Ser Gly Arg Lys Lys Gly Ser Val Leu Thr Ile Arg Leu Arg Ile  
115 120 125

Glu Thr Gln Met Glu Pro Pro Val Ala Ile Gly Pro Asn Lys Gly Leu  
130 135 140

Ala Glu Gln Gly Pro Pro Ile Gln Glu Gln Arg Pro Ser Pro Asn Pro  
145 150 155 160

Ser Asp Tyr Asn Thr Thr Ser Gly Ser Val Pro Thr Glu Pro Asn Ile  
165 170 175

Thr Ile Lys Thr Gly Ala Lys Leu Phe Ser Leu Ile Gln Gly Ala Phe  
180 185 190

Gln Ala Leu Asn Ser Thr Thr Pro Glu Ala Thr Ser Ser Cys Trp Leu  
195 200 205

Cys Leu Ala Ser Gly Pro Pro Tyr Tyr Glu Gly Met Ala  
210 215 220

<210> 8

<211> 203

<212> PRT

<213> porcine endogenous retrovirus Type PERV MSL

<400> 8

Asn Asn Gly Lys His Cys Gly Asn Pro Arg Asp Phe Phe Cys Lys Gln  
1 5 10 15

Trp Asn Cys Val Thr Ser Asn Asp Gly Tyr Trp Lys Trp Pro Thr Ser  
20 25 30

Gln Gln Asp Arg Val Ser Phe Ser Tyr Val Asn Thr Tyr Thr Ser Ser  
35 40 45

Gly Gln Phe Asn Tyr Leu Thr Trp Ile Arg Thr Gly Ser Pro Lys Cys  
50 55 60

Ser Pro Ser Asp Leu Asp Tyr Leu Lys Ile Ser Phe Thr Glu Lys Gly  
65 70 75 80

Lys Gln Glu Asn Ile Leu Lys Trp Val Asn Gly Met Ser Trp Gly Met  
85 90 95

Val Tyr Tyr Gly Gly Ser Gly Lys Gln Pro Gly Ser Ile Leu Thr Ile  
100 105 110

Arg Leu Lys Ile Asn Gln Leu Glu Pro Pro Met Ala Ile Gly Pro Asn  
115 120 125

Thr Val Leu Thr Gly Gln Arg Pro Pro Thr Gln Gly Pro Gly Pro Ser  
130 135 140

Ser Asn Ile Thr Ser Gly Ser Asp Pro Thr Glu Ser Asn Ser Thr Thr  
145 150 155 160

Lys Met Gly Ala Lys Leu Phe Ser Leu Ile Gln Gly Ala Phe Gln Ala  
165 170 175

Leu Asn Ser Thr Thr Pro Glu Ala Thr Ser Ser Cys Trp Leu Cys Leu  
180 185 190

Ala Ser Gly Pro Pro Tyr Tyr Glu Gly Met Ala  
195 200

<210> 9

<211> 203

<212> PRT

<213> porcine endogenous retrovirus Type Tsukuba

<400> 9

Asn Asn Gly Lys His Cys Gly Asn Pro Arg Asp Phe Phe Cys Lys Gln  
1 5 10 15

Trp Asn Cys Val Thr Ser Asn Asp Gly Tyr Trp Lys Trp Pro Thr Ser  
20 25 30

Gln Gln Asp Arg Val Ser Phe Ser Tyr Val Asn Thr Tyr Thr Ser Ser  
35 40 45

Gly Gln Phe Asn Tyr Leu Thr Trp Ile Arg Thr Gly Ser Pro Lys Cys  
50 55 60

Ser Pro Ser Asp Leu Asp Tyr Leu Lys Ile Ser Phe Thr Glu Lys Gly  
65 70 75 80

Lys Gln Glu Asn Ile Leu Lys Trp Val Asn Gly Met Ser Trp Gly Met  
85 90 95

Val Tyr Tyr Gly Gly Ser Gly Lys Gln Pro Gly Ser Ile Leu Thr Ile  
100 105 110

Arg Leu Lys Ile Asn Gln Leu Glu Pro Pro Met Ala Ile Gly Pro Asn  
115 120 125

Thr Val Leu Thr Gly Gln Arg Pro Pro Thr Gln Gly Pro Gly Pro Ser  
130 135 140

Ser Asn Ile Thr Ser Gly Ser Asp Pro Thr Glu Ser Ser Ser Thr Thr  
145 150 155 160

Lys Met Gly Ala Lys Leu Phe Ser Leu Ile Gln Gly Ala Phe Gln Ala  
165 170 175

Leu Asn Ser Thr Thr Pro Glu Ala Thr Ser Ser Cys Trp Leu Cys Leu  
180 185 190

Ala Leu Gly Pro Pro Tyr Tyr Glu Gly Met Ala  
195 200

<210> 10

<211> 221

<212> PRT

<213> porcine endogenous retrovirus Type PERV B

<400> 10

Glu Lys Glu Lys Tyr Cys Gly Gly Ser Gly Glu Ser Phe Cys Arg Arg  
1 5 10 15

Trp Ser Cys Val Thr Ser Asn Asp Gly Asp Trp Lys Trp Pro Ile Ser  
20 25 30

Leu Gln Asp Arg Val Lys Phe Ser Phe Val Asn Ser Gly Pro Gly Lys  
35 40 45

Tyr Lys Val Met Lys Leu Tyr Lys Asp Lys Ser Cys Ser Pro Ser Asp  
50 55 60

Leu Asp Tyr Leu Lys Ile Ser Phe Thr Glu Lys Gly Lys Gln Glu Asn  
65 70 75 80

Ile Gln Lys Trp Ile Asn Gly Met Ser Trp Gly Ile Val Phe Tyr Lys  
85 90 95

Tyr Gly Gly Gly Ala Gly Ser Thr Leu Thr Ile Arg Leu Arg Ile Glu  
100 105 110

Thr Gly Thr Glu Pro Pro Val Ala Val Gly Pro Asp Lys Val Leu Ala  
115 120 125

Glu Gln Gly Pro Pro Ala Leu Glu Pro Pro His Asn Leu Pro Val Pro  
130 135 140

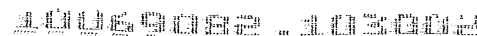
Gln Leu Thr Ser Leu Arg Pro Asp Ile Thr Gln Pro Pro Ser Asn Gly  
145 150 155 160

Thr Thr Gly Leu Ile Pro Thr Asn Thr Pro Arg Asn Ser Pro Gly Val  
165 170 175

Pro Val Lys Thr Gly Gln Arg Leu Phe Ser Leu Ile Gln Gly Ala Phe  
180 185 190

Gln Ala Ile Asn Ser Thr Asp Pro Asp Ala Thr Ser Ser Cys Trp Leu  
195 200 205

Cys Leu Ser Ser Gly Pro Pro Tyr Tyr Glu Gly Met Ala  
210 215 220



<210> 11

$\langle 211 \rangle$  220

<212> PRT

<213> porcine endogenous retrovirus Type PoEV1

<400> 11

Glu Lys Glu Lys Tyr Cys Gly Gly Ser Gly Glu Ser Phe Cys Arg Arg  
1 5 10 15

Trp Ser Cys Val Thr Ser Asn Asp Gly Asp Trp Lys Trp Pro Ile Ser  
20 25 30

Leu Gln Asp Arg Val Lys Phe Ser Phe Val Asn Ser Gly Pro Gly Lys  
35 40 45

Tyr Lys Met Met Lys Leu Tyr Lys Asp Lys Ser Cys Ser Pro Ser Asp  
50 55 60

Leu Asp Tyr Leu Lys Ile Ser Phe Thr Glu Arg Lys Thr Gly Lys Tyr  
65 70 75 80

Ser Lys Val Asp Lys Trp Tyr Glu Leu Gly Asn Ser Phe Leu Leu Tyr  
85 90 95

Gly Gly Gly Ala Gly Ser Thr Leu Thr Ile Arg Leu Arg Ile Glu Thr  
100 105 110

Gly Thr Glu Pro Pro Val Ala Met Gly Pro Asp Lys Val Leu Ala Glu  
115 120 125

Gln Gly Pro Pro Ala Leu Glu Pro Pro His Asn Leu Pro Val Pro Gln  
130 135 140

Leu Thr Ser Leu Arg Pro Asp Ile Thr Gln Pro Pro Ser Asn Ser Thr  
145 150 155 160

Thr Gly Leu Ile Pro Thr Asn Thr Pro Arg Asn Ser Pro Gly Val Pro  
165 170 175

Val Lys Thr Gly Gln Arg Leu Phe Ser Leu Ile Gln Gly Ala Phe Gln  
180 185 190

Ala Ile Asn Ser Thr Asp Pro Asp Ala Thr Ser Ser Cys Trp Leu Cys  
195 200 205

Leu Ser Ser Gly Pro Pro Tyr Tyr Glu Gly Met Ala  
210 215 220

<210> 12

<211> 15

<212> PRT

<213> porcine endogenous retrovirus

<400> 12

Arg Glu Glu Arg Arg Asp Arg Arg Gln Glu Lys Asn Leu Thr Lys  
1 5 10 15

<210> 13

<211> 14

<212> PRT

<213> porcine endogenous retrovirus

<400> 13

Ala Arg Asn Cys Pro Lys Lys Gly Asn Lys Gly Pro Lys Val  
1 5 10

<210> 14

<211> 16

<212> PRT

<213> porcine endogenous retrovirus Type PoEV1

<400> 14

Thr Ser Leu Arg Pro Asp Ile Thr Gln Pro Pro Ser Asn Ser Thr Thr  
1 5 10 15

<210> 15

<211> 15

<212> PRT

<213> porcine endogenous retrovirus Type PERV B

<400> 15

Lys Gly Lys Gln Glu Asn Ile Gln Lys Trp Ile Asn Gly Met Ser  
1 5 10 15

<210> 16

<211> 18

<212> PRT

<213> porcine endogenous retrovirus Type PoEV1

[illegible]

<400> 16

Arg Lys Thr Gly Lys Tyr Ser Lys Val Asp Lys Trp Tyr Glu Leu Gly  
1 5 10 15

Asn Ser

<210> 17

<211> 12

<212> PRT

<213> porcine endogenous retrovirus Type Tsukuba

<400> 17

Asn Thr Val Leu Thr Gly Gln Arg Pro Pro Thr Gln  
1 5 10

<210> 18

&lt;211&gt; 22

<212> PRT

<213> porcine endogenous retrovirus Type PERV A

<400> 18

Gly His Gly Arg Trp Lys Asp Trp Gln Gln Arg Val Gln Lys Asp Val  
1 5 10 15

Arg Asn Lys Gln Ile Ser  
20

<210> 19

<211> 16

&lt;212&gt; PRT

<213> porcine endogenous retrovirus Type PERV A

&lt;400&gt; 19

Ile Gln Glu Gln Arg Pro Ser Pro Asn Pro Ser Asp Tyr Asn Thr Thr  
1 5 10 15